VOL. 108 • NO. 2814 • PAGES 615-642

December 3, 1948

Science

Prehistoric Eskimo Dwelling, Baffin Island

(See page 641)

FISHER

Isotemp OVENS

Provide

Constant, Uniform Heat

The Fisher Isotemp Oven provides constant, uniform temperatures throughout the entire oven chamber. Its heating range of 35° to 200° C. can be thermostatically controlled to within ±0.5° C.

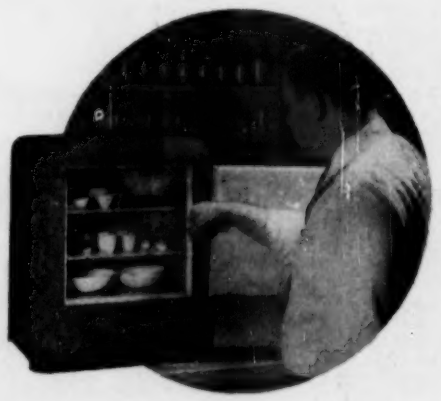
The sheet aluminum oven chamber is 12 inches square by 12½ inches deep, providing a total useful three-shelf area of 430 square inches.

The nickel-chromium heating elements are embedded outside the oven chamber; the thermostat contacts are sealed in a metal capsule and the door opens automatically under pressure.

Furnished with three shelves and thermometer, for 115 volt A.C., or for 230 volt A.C..... **$125.00**

(Specify voltage when ordering)

The Isotemp Oven has a cast aluminum frame; it serves equally well for heating, drying and sterilizing.



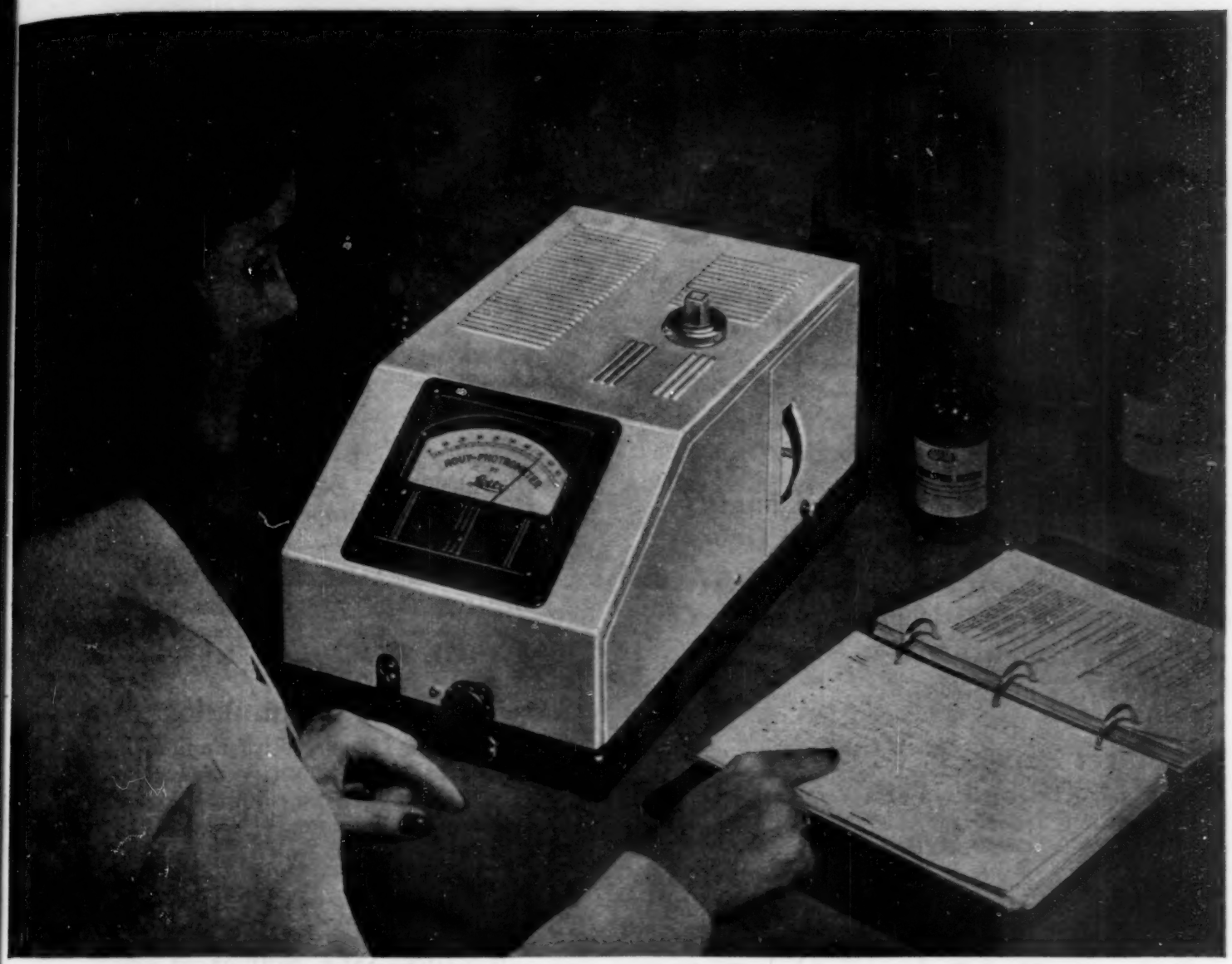
Placement of heaters, complete insulation and high thermal conductivity of aluminum interior result in uniform temperature on all three shelves—front to back.

Manufacturers—Distributors

FISHER SCIENTIFIC CO.
717 Forbes St., Pittsburgh (19), Pa.
2109 Locust St., St. Louis (3), Mo.

EIMER AND AMEND
Greenwich and Morton Streets
New York (14), New York

Headquarters for Laboratory Supplies



the Leitz Rouy Photrometer

The Rouy Photrometer by Leitz is the result of 2½ years of research and development. It has been constructed with the same skill and precision which have always been associated with any product bearing the trademark of E. Leitz, Inc.

Already calibrated for 38 of the most common clinical tests, the Rouy Photrometer by Leitz is simple to operate; no special skill is required of the user.

Each Leitz Photrometer is individually calibrated, and is used with its individual handbook—prepared by Leitz technicians.

Through our Solution Supply Service, Reagents especially prepared for these determinations are available for your convenience.

E. LEITZ, INC.

THE MAKERS OF LEICA CAMERAS

304 HUDSON STREET
NEW YORK 13, N. Y.

MICROSCOPES, PHOTROMETERS AND OTHER SCIENTIFIC INSTRUMENTS

E. LEITZ, INC., Dept. 503 304 Hudson St., New York 13, N. Y.

Please send me information on:

☐ Leitz Photrometers ☐ Solution Supply Service

NAME_____

ADDRESS_____

CITY_____ STATE_____

MY DEALER IS_____

Science

AAAS EDITORIAL BOARD
(*Terms expire July 31, 1949*)
Arthur Bevan Bentley Glass Malcolm Soule
Edward Condon Everett Wallis
George Baitsell, *Editor-in-Chief*
Mildred Atwood Rustigan
Executive Editor of Science
Advertising Representative, F. A. Moulton

Vol. 108 No. 2814 Friday, December 3, 1948

CONTENTS

(Cover photo by courtesy of Henry B. Collins, Jr.)

Science, a weekly journal, is published each Friday by the American Association for the Advancement of Science at The Business Press, Incorporated, N. Queen St. and McGovern Ave., Lancaster, Pa. Founded in 1880, it has been since 1900 the official publication of the AAAS. Editorial and Advertising Offices, 1515 Massachusetts Avenue, N.W., Washington 5, D. C. Telephone, EXecutive 6060 or 6061. Cable address, SCIMAG, Washington, D. C. Entered as second-class matter at the Post Office at Lancaster, Pa., January 13, 1948, under the Act of March 3, 1879. Acceptance for mailing at the special rate postage provided for in the Act of February 28, 1925, embodied in paragraph 4, Sec. 538, P. L. and R., authorized January 13, 1948.

Articles offered for publication should be sent to the Editor. The AAAS assumes no responsibility for the opinions expressed by contributors. Membership correspondence for the AAAS should be sent to the Administrative Secretary.

Annual subscription, $7.50; single copies, $.25; foreign postage (outside the Pan-American Union), $1.00 extra; Canadian postage, $.50 extra. Remittances and orders for subscription and single copies should be sent to the Circulation Department, AAAS, North Queen Street and McGovern Avenue, Lancaster, Pennsylvania, and 1515 Massachusetts Avenue, N.W., Washington 5, D. C. Claims for missing numbers will not be allowed if received more than 60 days from date of issue. No claims allowed from subscribers in Central Europe, Asia, or the Pacific Islands other than Hawaii or because of failure to notify the Circulation Department of a change of address or because copy is missing from the files.

Change of address. Four weeks notice is required for change of address. This should be sent to *Science*, 1515 Massachusetts Avenue, N.W., Washington 5, D. C. When ordering a change, please furnish an address stencil label from a recent issue. Address changes can be made only if the old as well as the new address is supplied.

The American Association for the Advancement of Science also publishes *The Scientific Monthly*. Subscription rates on request.

The Effects of Changes in Quantity, Combination, and Position of Genes

Curt Stern
Department of Zoology, University of California, Berkeley

THAT WE KNOW OF THE EXISTENCE OF GENES is intimately bound up with the fact that genic species occur in different varieties. If all mankind had identical eye color, no knowledge of eye-color genes would have been obtained. As it is, the differences between the eye colors of different individuals can be traced back to differences in causal agents, located at a specific region in a specific chromosome of these individuals. In one individual the specific region, or locus, controls, in collaboration with other agents, the developmental processes which lead to the appearance of one type of eye color; in another individual the same region exerts a control which leads to the development of another type of eye color. This region, or locus, we call the "gene," and its different varieties, as present in different homologous chromosomes, we call the "alleles" of the gene. What the gene consists of, or what distinguishes it from other genes at other loci, remains an unsolved problem. What the differences between alleles consist of remains likewise beyond the scope of the discovery that there *are* different alleles.

In its final form the problem of the nature of genes and their allelic varieties belongs in the sphere of the chemist. Someday, structural formulas will be available which describe the constitution of different genic species and their allelic varieties. At that time we will also understand in detail how the gene molecules, or molecular complexes, interact with their immediate cellular surroundings and initiate, or control, or enter into reactions which are part of the multidimensional network of processes which constitute cellular metabolism and development. The biochemical analysis of these processes themselves may lead us backward until primary genic action is reached. In particular, the biochemistry of metabolic differences caused by different alleles has led to most significant results and suggestive interpretations. Very likely certain initial reactions which the wild type strains of *Neurospora* can, and which strains with mutant alleles cannot, perform are very close to the gene end of reaction sequences. How close remains undecided, since it does not become obvious when the tracing backward of reactions has reached the unknown gene.

The geneticist can employ some methods of manipulating the conditions at the gene end. He can vary the quantities of given alleles present in the cells; he can assemble combinations of different alleles; and he can cause shifts in the position of genes within the chromosomal system. From determinations of the effects of such manipulations certain statements can be made about the reactions leading to the effects. Such analyses do not lead to specific recognition of the reactions but rather to knowledge of certain general characteristics. As in the discovery that there *are* genes and alleles, which falls short of showing *what* these entities are, the manipulation of gene quantities, combinations, and chromosomal positions will lead to recognition of some attributes of genic reactions but not to the reactions themselves. Undoubtedly, some day the biochemical and the genetic approaches will be combined in suitable material.

The following discussion will survey results of the genetic approach. Different workers, particularly R. Goldschmidt (*2*) and Sewall Wright (*11*), have contributed data and interpretations in this field. Instead of attempting a general summary, this paper will deal with one locus only, namely, the gene cubitus interruptus, ci, in *Drosophila melanogaster* (*3–10*). This gene is concerned with the formation of the fourth (cubital) vein on the wing of the fruit fly. The effect, under various genetic and environmental conditions, ranges from complete absence of the distal section of the vein, over the absence of only parts of this section, to its complete presence. By determining the length of the vein fraction present, one can read off the genic effect in a quantitative way—though it should not be supposed that primary gene effect and terminal vein effect are linearly related.

The ci locus is suitable for dosage studies since it is part of the small "fourth" dot chromosome which can be obtained in quantities from one to three in otherwise diploid flies. Furthermore, it is not necessary to study flies distinguished by the number of whole dot chromosomes. Dot chromosomes are available in which a short middle section, which includes the ci

This paper was one of those presented in the Symposium on Genes and Cytoplasm, held on September 14, during the Centennial Celebration of the AAAS in Washington, D. C.

locus, is lacking. By the use of these deficient chromosomes a series of quantities of the ci locus can be built up, namely, one dose (one nondeficient chromosome, one or two deficient chromosomes), two doses (two nondeficient chromosomes, none or one deficient chromosome), and three doses (three nondeficient chromosomes). These dosage studies were carried out on different alleles of the ci gene. For the typical mutant allele ci, gene quantity and presence of venation are positively correlated: the more genes, the more vein is formed (Fig. 1, middle).

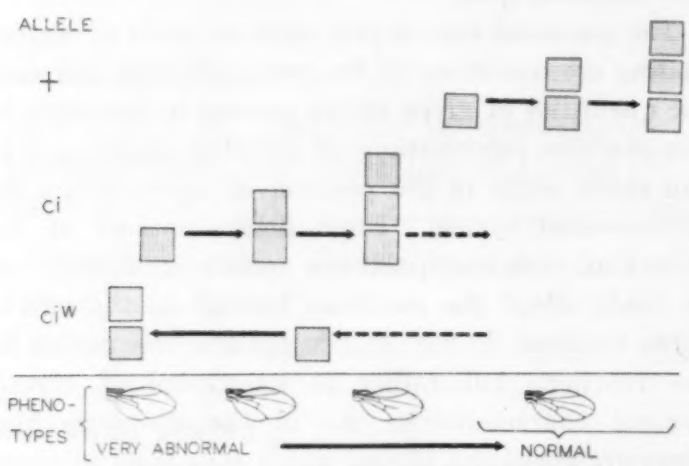


FIG. 1. The effect of different doses of the alleles +, ci, and ci^{W} on venation in *Drosophila melanogaster*.

While the name cubitus interruptus might suggest that the allele ci is an active agent causing vein *interruption*, the dosage data show that the ci allele works toward the same effect of presence of venation as does the normal allele. However, even three ci alleles, while they approach it, are not yet sufficient to accomplish normality.

It fits in well with this result that a single quantity of a wild type normal allele of ci does not cause complete venation. Such normality requires two doses of a normal allele for its production. The effect on venation of three doses of a wild type allele does not go beyond that of two (Fig. 1, top).

The dosage studies of wild type alleles led to a further finding—that of different kinds of normal alleles. Each of them, in double dose, causes full venation, but by single doses different degrees of incompleteness of vein are produced.

A strikingly different dosage effect is observed with the mutant allele ci^{W}. A single quantity of ci^{W} results in a fairly high amount of vein material. Two ci^{W} alleles, on the other hand, decrease this amount greatly (Fig. 1, bottom).

What may be deduced from these dosage data as to basic genic action? We visualize such action as taking place beween the chromosomal gene and a cellular—probably intranuclear—substrate S (Fig. 2). The fact that increased quantities of from one to three doses of the mutant ci allele result in increased venation means that S is present in excess

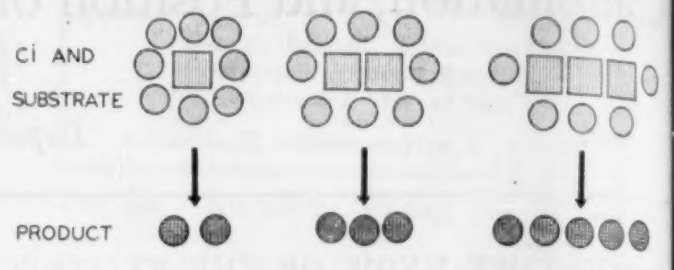


FIG. 2. An interpretation of the dosage effect of the ci allele in terms of substrate and different amounts of product.

of the amount turned over by one or two of these alleles. Furthermore, the simplest assumption regarding the product, P, of the interaction of ci and S is that P enters a chain of reactions which is positively correlated with the sequence of developmental processes leading to appearance of venation. It is also apparent that whatever the number of links in this chain of reactions is, no threshold effects occur which obliterate the result of the differences in amount of P which, in turn, are caused by the dosage differences of ci. These deductions are independent of specific hypotheses of gene action. If primary gene action should consist of production of total or partial replicas of genes which are sent into the cytoplasm and there enter metabolic and developmental processes, then P would represent these replicas.

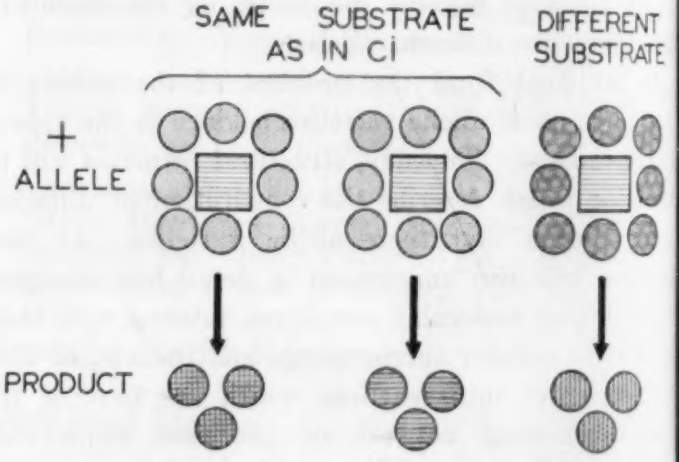


FIG. 3. Alternative interpretations of the difference in effect of the + and the ci allele: left, same substrate for + as in ci, and same product, in increased quantity as compared to ci; middle, same substrate for + as in ci, but different product; right, different substrate for + than in ci, and different product.

The dosage effect of normal alleles of the ci locus implies, again, excess of substrate present in the nucleus beyond the amount turned over by one dose. The absence of a phenotypic difference between organisms with two and three normal gene quantities shows that a limit is reached. Whether this limit is due to restriction of primary substrate or restrictions at later developmental stages remains unknown.

A comparison of the action of a normal, +, and the mutant, ci, allele involves assumptions regarding the substrate and the primary product (Fig. 3). Assuming that an allele utilizes a single substrate, it could either be that the two different alleles use the same substrate, S, or that they use different substrates, S_+ and S_{ci}. In the former case two possibilities exist in regard to the primary product. Both alleles may transform the same S into identical Ps, but in different amounts, or specifically different products, P_+ and P_{ci}, may be formed. The formation of qualitatively different products is also most likely, should the two alleles use different substrates, S_+ and S_{ci}. Whatever the situation, it is necessary to explain the similar, though quantitatively graded, action of the two alleles. With identical P, a lower rate of production under the influence of ci as compared to + is sufficient to account for the facts. With different P_+ and P_{ci}, the situation would be similar to that met in a great variety of physiological studies in which chemically related substances produce metabolic or developmental effects which can be arranged in a quantitative series.

The dosage effect of the ci^W allele, which leads to decrease instead of increase of venation with increasing gene quantity does not so readily fit into the schemes outlined. It is unlikely that ci^W produces the same kind of P as either one or both + and ci. This assumption could be made only if one is willing to postulate a relation between quantity of P and vein effect, such as to yield similar effects with large and small quantities but unlike effects with intermediate quantities. While such relations are not unknown in pharmacological studies, known variations of quantity in genic dosage studies have always shown simple relations between increase of gene quantity and increase of effect (often up to a maximum beyond which no further changes in effect take place). Admittedly such dosage studies are few in number, and the hypothesis of ci^W producing the same kind of P, but in a quantity outside of the range of those produced by the known doses of ci and +, cannot be disproven. However, in the light of further facts to be quoted below the hypothesis of identical primary products of various alleles would probably involve a whole series of maxima and minima of effects in relation to quantity of P and thus become increasingly improbable.

If ci^W results in a specific $P_{ci}{}^W$ unlike P_+ and P_{ci}, an explanation of why two $P_{ci}{}^W$s cause less venation than one $P_{ci}{}^W$ is still required. One might assume a destructive property of $P_{ci}{}^W$ in regard to the processes which lead to venation. This would mean that processes resulting in presence of the vein go on independently of the ci locus and that the alleles + and ci accelerate these processes while the alleles ci^W and ci^D (this latter will not be dealt with here) slow them down. One might either acquiesce with such a concept or try to fit it into a more unified picture. Considering the presumptive similarity of alleles of the same genic species, one might prefer a picture of basically similar, though quantitatively different, effects of different alleles. Such a picture would permit variations in effect from zero to some positive or negative value but not *both* positive and negative ones. As a specific illustration it might be assumed that the ci^W allele

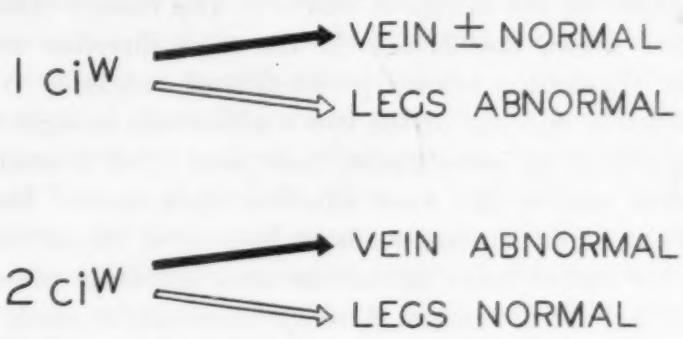


FIG. 4. Dosage effect of ciW on vein and legs.

controls two different processes, one leading toward (positive) production of venation and the other toward an unrelated phenotype. Assuming further that these two processes interfere with each other, a scheme could be developed according to which an increase in dose of ci^W strengthens the reaction to the unrelated phenotype at the cost of the vein reaction, resulting in a negative correlation between vein effect and gene quantity. Such a scheme is not completely without foundation, since the ci^W allele strikingly affects leg and bristle formation in contrast to the + and ci alleles, which, with every dose, lead to normal legs and bristles (Fig. 4). A single ci^W dose, while making for nearly normal venation, causes crippled legs and extra bristles; a double dose of ci^W reverses the situation, leaving a great gap in the vein but permitting nearly normal legs and bristles.

The data on effects of different doses of alleles take on a new aspect when combinations of different alleles are considered. In general, heterozygotes between two alleles either appear phenotypically similar to one of the homozygotes or show an intermediate phenotype. Conforming to these rules, the venation shown by ci/+ flies is intermediate between ci/ci and +/+, and ci^W/+ flies are intermediate between ci^W/ci^W and +/+. The heterozygotes ci/ci^W are close to ci^W/ci^W phenotypically. It thus appears as if the action of heterozygotes may be interpreted in terms of independent action of their constituent alleles, e.g. two doses of ci cause a certain small amount of

venation, two doses of + a large one, and the combiation of one dose of each results in an intermediate venation. This simple interpretation proves insufficient if a comparison is made not between heterozygotes and the homozygotes of their constituent alleles but rather with their constituent hemizygotes. It now turns out that heterozygotes ci/+ are less normal than the hemizygotes +/0. The most striking case of this nature is found if a certain normal allele, $+^3$, is employed. Homozygotes $+^3/+^3$ are normal, and nearly all $+^3$ hemizygotes are likewise so. More than 40% of the ci/$+^3$ flies, however, show incomplete venation. This constitutes an interference in the action of the alleles ci and $+^3$. The dosage studies had shown that ci acts in the same direction as + or $+^3$, namely, toward production of venation. Yet, when ci and one of the two + alleles are brought together in the same nuclei, their joint effect is smaller than that of the more effective allele alone. These facts might suggest some mechanism of competition. If + and ci make use of the same substrate present in a limited amount, a competition might result in which the ci allele deprives the + allele of its full share. If the ci allele turned the substrate over more slowly or less efficiently into the effective product P than the + allele, the joint action of the two alleles might be less than that of the "better" one alone. Should the two alleles lead to the production of different P_{ci} and P_+ substances, then the competition would not necessarily occur at the primary gene action-level but could also take place at a later stage of the genic reaction chain where P_{ci} and P_+, or their further derivatives, might compete for substrates. While the idea of competition at the gene level was earlier placed by the writer into the foreground, new data to be reviewed below suggest that a later stage is involved. In view of the unknown nature of the interaction between the different alleles, it now appears preferable to use the more descriptive, general term, interference. Competition may or may not constitute the mechanism of interference.

The type of effect of the ci/ci^w heterozygote is similar to, but much more extreme than, that of ci/+. The legs and bristles of ci/ci^w are normal, but the vein greatly deficient. In other words, the presence of the ci allele, instead of "adding" its share of vein production to that of the hemizygous ci^w allele, which in single dose causes a high degree of venation, results in an interference in gene action, leaving the vein nearly unformed. Most striking is the interference in the last combination to be discussed here, that of + and ci^w (Fig. 5). The hemizygotes of both these alleles appear normal in venation or close to it, whereas the heterozygotes ci^w/+ have greatly deficient veins. This case demonstrates not only that the interference phenomenon consists of an effect of one of the two alleles on the other but that it is a mutual interference of the two alleles since the heterozygote is less normal than either hemizygote.

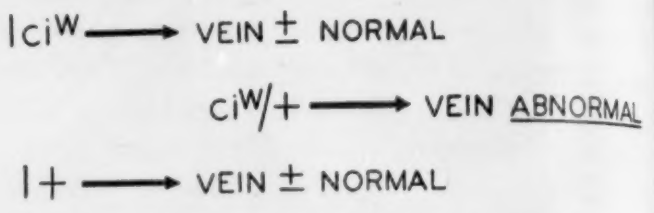


FIG. 5. Interference between + and ci^w.

The final manipulation of events at the gene end of the chain of genic action to be discussed consists of altering the chromosomal neighborhood of the ci locus. This can be done either by transferring a section of the dot chromosome which includes the ci locus to another chromosome or by removing part of the dot chromosome, exclusive of the ci locus, and replacing it by a section from another chromosome. Both methods of changing the position of the ci locus relative to neighboring chromosomal regions were used. Changing the position of a + allele gave rise to a number of rearrangements called R(+), with superscripts [$R^1(+)$, $R^2(+)$, etc.] denoting the different rearrangements as discovered one after the other in cultures derived from X-ray-treated flies. Changing the position of the ci allele similarly provided series of "position alleles R(ci)." R(+) alleles had first been studied by Dubinin and Sidorov, who discovered that homozygotes R(+)/R(+) and hemizygotes R(+) lead to normal venation just as the unchanged + allele, but that heterozygotes of many position alleles R(+) with the ci allele, R(+)/ci, show deficient venation. The observations seemed at first strange and peculiar to position alleles. It is now clear that these relations are quite similar to those characteristic for combinations of nonposition alleles as described above. They are an expression of interference phenomena which make combinations of alleles less effective in terms of venation than single doses of the alleles by themselves. The degree of interference varies with the kind of R(+) allele involved. Among 17 different R(+) alleles tested in our laboratory, interference was so strong in 4 cases that the heterozygotes R(+)/ci were more deficient in venation than either homozygote R(+)/R(+) or ci/ci. In the other 13 cases the degree of interference was less, making the heterozygote venation-deficient, though less or not more so than the homozygote with high vein deficiency, ci/ci. And to make the similarity with a nonposition allele, ci^w, still greater, one of the R(+) alleles, $R^2(+)$, turned out to cause

normal phenotype in hemozygous but deficient ci/ci-like venation in the homozygous state.

When position alleles of the mutant ci allele were produced, new facts came to light. No comprehensive survey can be given at present which covers the more than 40 different R(ci) alleles which have been tested. Dosage studies were made with a few of those that proved to be viable in homo- and hemizygous doses. (Rearrangements frequently are associated with recessive lethals.) With only one exception the R(ci)/R(ci) homozygotes studied did not cause the appearance of less veins than the ci/ci constitution, while several proved to be more effective in vein formation than ci/ci. Some of these R(ci) alleles—for instance, R^{29}(ci)—while leading to less than normal venation in double dose, lead to fuller venation, in some cases nearly normal, in single dose.

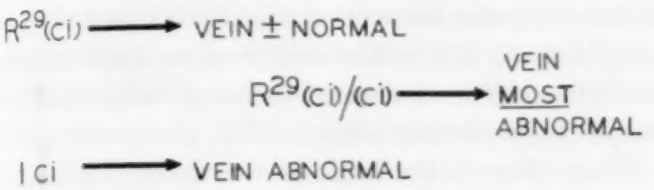


FIG. 6. Interference between R^{29}(ci) and ci.

Yet, in combination with both ci or a + allele—that is, as R(ci)/ci and R(ci)/+ heterozygotes, these same as well as nearly all other R(ci) alleles lead to more deficient venation than ci/ci and ci/+, respectively. In some case, as in R^{29}(ci)/(ci), the amount of vein present was less than in either of the two constituent hemizygotes R^{29}(ci) or ci (Fig. 6). Thus, again we meet the interference phenomenon in its extreme, clearly mutual expression.

One further fact appeared in studies of recombinations involving position alleles. When the R(ci) alleles were arranged in order of increasing effectiveness in vein production, if combined in heterozygotes with a + allele, and this arrangement was compared with one based on increasing effectiveness in vein production, if the R(ci) alleles were combined with the ci allele, it was found that the two arrangements did not follow the same order. For example, R^{52}(ci)/+ leads to more venation than R^{18}(ci)/+, but R^{52}(ci)/ci to less venation than R^{18}(ci)/ci.

What distinguishes the position alleles from the nonposition alleles which gave rise to them, and what differentiates the different R(+) and the different R(ci) position alleles from each other? No final answer to these questions seems to be available, but it is at least possible to suggest which apparent answers fail to solve these problems. The change which transforms a normally located allele into a position allele is of a different nature from mutant changes which transform alleles. The latter are caused by changes directly at the locus in question, and they are essentially irreversible. The former may be caused by breakage at considerable distance from the locus and replacement of the normally neighboring chromosomal material by different chromosomal material, and the change in the action of the gene reverts immediately when its normal position is restored. It appears, thus, that position alleles owe their properties not to intrinsic alterations of the original alleles but to changes in their chromosomal environment.

A simple hypothesis which might be invoked is the assumption that the specific substrate for each gene is present in a specific concentration in the neighborhood of a normally located gene but in a different concentration in those other regions to which the gene had been shifted. Such a hypothesis would account for the whole range of effects of different position alleles according to range of concentrations of the substrate. This idea has met with great difficulties as more data have become available. Since nearly all R(ci)/+ heterozygotes cause less venation than ci/+, one would assume that in general the concentration of the substrate is less at the R(ci) loci than at the ci locus. Why, then, do some of these R(ci) homo- and hemizygotes cause more venation than ci/ci and ci? If the lesser amount of venation in R^{18}(ci)/+ as compared with R^{52}(ci)/+ were due to greater limitation of substrate at the R^{18}(ci) than at the R^{52}(ci) locus, why does R^{18}(ci)/ci make for more vein than R^{52}(ci)/ci? Furthermore, the observed interference from position allele to normally located allele in terms of the hypothesis of changed quantity of substrate would reasonably imply a sharing of the localized substrate by the two alleles, interference being the result of increased competition for a more limited quantity of the substrate. But if the R(ci) alleles had retained their original ci-like attributes, they should behave in R(ci)/ci heterozygotes toward ci as typical ci alleles in an additive, but not an interfering way. Finally, there is evidence against the concept of direct sharing of a localized substrate. Such sharing would involve very close spatial approximation of the two alleles within the nuclei of heterozygotes. In *Drosophila,* approximation of homologous chromosome regions is indeed normally present due to somatic pairing. There are, however, exceptions to this rule. In our collection of position alleles there occur two in which the chromosomal rearrangement consists of the removal of a short middle section from the dot chromosome, including the ci locus, and the insertion of this section

into another chromosome (Fig. 7). In heterozygotes in which one dot chromosome is typically whole while the other is "divided up" into the deficient dot chromosome and the insertion within another chromosome, no pairing takes place between the insertion and its homologous region in the complete dot chromosome. Yet, interference between position allele and

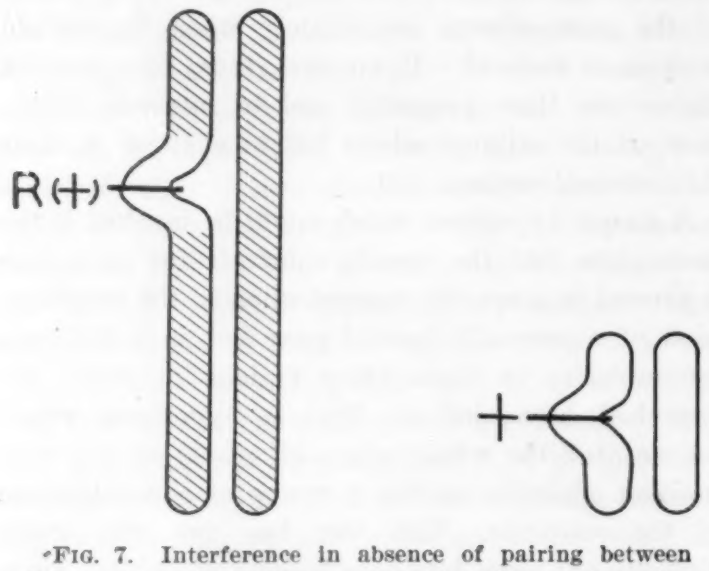


FIG. 7. Interference in absence of pairing between R(+) and +: left, chromosome pair with an insertion R(+) into one homologue from chromosome 4; right, chromosome pair 4, with one homologue deficient for the translocated R(+) section.

normally located allele occurs in typical fashion. This shows that close proximity is not necessary for the interference of position alleles with the action of normally located alleles.

The significance of these and other cases of position alleles in which no immediate proximity exists between the interfering alleles goes beyond its bearing on the hypothesis of substrate limitation. It shows that whatever the nature of interference is, it acts over distances which exclude a direct inhibition from gene to gene. Interference, if its site is the chromosomal locus, either must be mediated by the primary or derived gene products or takes place at a later stage in the reaction sequence or outside the nucleus between gene-dependent products.

Some years ago Ephrussi and Sutton (*1*) proposed an ingenious, different scheme to account for the properties of position alleles. They pictured genes as chain-like molecules which, under the influence of forces in their environment, could assume folded and unfolded configurations. These different configurations would endow the genes with different activities. Position alleles, particularly in heterozygous combinations with normally located alleles, were regarded as less extended and therefore less reactive chains than nonposition alleles. In order to account not only for the decreased activity of position alleles but also for their interference with the activity of the normally located alleles, a specification of the molecular fol ing theory was made. It was assumed that the pa ing forces between homologous chromosomal regio in *Drosophila* are responsible for the degree molecular folding, normal pairing resulting in norm extension of the two alleles, and pairing stresses, d to structural heterozygosity in case of position all heterozygotes, resulting in reduced extension. One the merits of this hypothesis is that it can account f reduced activity of the normally located allele und the influence of the abnormal pairing forces exer by a position allele and its chromosomal neighbo hood. There are, however, various facts which not fit the scheme. Here we shall refer only to t same observations which also were in conflict wi expectation derived from the hypothesis of variabl amounts of substrate. As in that hypothesis, the id of abnormal pairing forces as a basis for interfere in heterozygotes between a position allele and a no mally located allele demands a close approximati of the two. The absence of such approximation is n compatible with that idea.

What, then, is the basis of the changed activity position alleles? One might speculate to the effe that different positions provide an allele with qualit tively different substrates with which it can inter In this fashion the problem of not simply quanti tively related differences of genic action, in dosag in combination, and in position experiments, is pass on to the hypothetical level of not simply quanti tively different gene-substrate relations.

There is one suggestion of a particular chromoso neighborhood being different from all others. It w stated above that most R(ci) alleles in heterozygot with ci result in less vein production than in the ca of ci/ci. There are 6 R(ci) alleles which fall out line, since they have consistently shown a greater ve amount in R(ci)/ci heterozygotes than ci/ci. The are the only cases in which the ci locus had been l in the dot chromosome but the tip of the chromoso had been replaced by a section of the right arm chromosome 2. In 5 rearrangements the break i chromosome 2 was located (strangely enough!) with the limited region 45–48 as defined in Bridges' saliva chromosome map. In the sixth the break in chrom some 2 was in region 58. It appears from these da that the right arm of chromosome 2 is peculiarly di ferent from other chromosomes. The nature of th difference is not apparent, but it is not of the sa type as that between eu- and heterochromatin. T latter two kinds of chromosomal materials act diffe ently from each other if brought into changed rel tion with a position allele. Strongly altered ge effects of the ci locus are produced only by transf

ring it into euchromatic regions, while heterochromatic regions alter the effects of position alleles either little or not at all.

We may summarize the main points briefly:

(1) One, two, or three doses of an allele may produce different effects. This means excess of substrate beyond that used in normal diploid cells. Some alleles act, with different degrees of success, toward normal venation; others, toward abnormal venation. In the latter case different competing reactions controlled by the same allele may be involved.

(2) Combinations of two alleles may be less effective than the "better" of the two or than either alone. There is, thus, not additive action of two alleles but interference, in some cases clearly of mutual nature.

(3) Position alleles also show interference with normally located alleles of their own kind. If different position alleles are arranged in two series according to grade of effect when they are heterozygous for a normal or a mutant allele, it is found that the two seriations do not agree with each other. It seems that qualitatively different phenomena are involved in the shifting of an allele to different positions.

(4) Certain chromosome regions have specific properties causing a specific type of position effect.

If we look back at the material presented, it appears that much can be learned still by genetic methods about the action and interaction of alleles. The genetic analysis, in spite of its lack of biochemical precision, remains at present a more delicate tool for the probing of immediate genic action than even the most advanced methods of the microanalyst. But the vagueness of the geneticist's results lets us look forward eagerly to the time when the biochemist has caught up with him.

References

1. Ephrussi, B., and Sutton, E. *Proc. nat. Acad. Sci., Wash.*, 1944, **30**, 183–197.
2. Goldschmidt, R. *Physiological genetics.* New York: McGraw-Hill, 1938.
3. Stern, C. *Genetics*, 1943, **28**, 441–475.
4. Stern, C. *Genetics*, 1948, **33**, 215–219.
5. Stern, C. Unpublished data.
6. Stern, C., and Heidenthal, G. *Proc. nat. Acad. Sci., Wash.*, 1944, **30**, 197–205.
7. Stern, C., MacKnight, R. H., and Kodani, M. *Genetics*, 1946, **31**, 598–619.
8. Stern, C., and Schaeffer, E. W. *Proc. nat. Acad. Sci., Wash.*, 1943, **29**, 351–361.
9. Stern, C., and Schaeffer, E. W. *Proc. nat. Acad. Sci., Wash.*, 1943, **29**, 361–367.
10. Stern, C., Schaeffer, E. W., and Heidenthal, G. *Proc. nat. Acad. Sci., Wash.*, 1946, **32**, 26–33.
11. Wright, S. *Physiol. Revs.*, 1941, **21**, 487–527.

Foreword From *Vernalization and Photoperiodism*

Kenneth V. Thimann
Harvard University

IT IS AN HONOR TO BE ASKED TO CONTRIBUTE a foreword to this stimulating publication. The book, of course, owes its inception to Dr. Verdoorn's enthusiastic interest in the documentation of plant science. As a matter of history, it is the last of a series of titles which were originally announced by him before the war and have one by one been published during the last seven years. The authors of these chapters have cooperated generously and have produced conscientious and thorough reviews of their several fields. They are authoritative and familiar with the ramifications of the work they discuss. One of them is himself the author of a book in the same general field (*8*). At the moment, therefore, these comprise almost the last word.

Nevertheless, although the present seems a particularly opportune moment for the appearance of this book, there can be no doubt that in this field, which is developing so rapidly, fundamental changes in outlook might well come at any moment. Such a highly flexible situation is of course typical of experimental plant science, which in many respects is still somewhat embryonic, but it is perhaps particularly so of the branches of plant physiology and agronomy which are discussed here.

The reasons for this are basically simple. The physiology of flowering, with which this book deals, has as yet no basis in the general physiology and biochemistry of the plant. The fundamental discoveries on which it rests are the effects of the chilling of germinating seeds and of the varying of the length of day in mature plants approaching the stage of "readiness to flower (Blühreife)." Both of these are essentially *ad hoc* discoveries which did not arise directly from a continuing chain of closely-knit research and deduction, such as, for instance, that on which genetics rests today, or even that which led

This foreword from *Vernalization and photoperiodism: a symposium*, by A. E. Murneek, R. O. Whyte, *et al.* (Waltham, Mass.: Chronica Botanica; New York: Stechert Hafner, 1948. Pp. xiv + 196. $4.50), is reprinted in *Science* by permission of the author and the Chronica Botanica Company.

to our rather extensive knowledge of the auxins. They have inspired a large amount of experiment and have led to very important practical applications in the agriculture of both temperate and tropical zones, which are discussed in the several chapters of this book. But the underlying problems are difficult to attack and, indeed, it is not quite clear that they can even be formulated. What, for instance, is the nature of the change from the vegetative to the flowering state? Is it localized in the buds themselves, as would be implied by the concept of a flowering hormone, of which the buds would be the receptors, or is it systemic—a symptom of an inner complete change in metabolism, as in the theory of phasic development? Curiously enough, these two viewpoints have each become associated with one of the two main fields of endeavor, namely, photoperiodism and vernalization, respectively.

Only recently have these two basic ideas shown signs of approaching one another. It should be pointed out that the demonstration by Gregory and Purvis that vernalization of cereals may be reversed points in the general direction of control by special substances rather than by the successive completion of determinative "phases." However, it is important to note that Sen and Chakravarti (*5*) have been unable to reverse the vernalization of mustard either by high temperature or by dry storage for a year. Mustard differs, however, from rye in that the excised embryos can be fully vernalized in pure water, while rye embryos require sugar for complete and rapid vernalization. Whether there is any connection between this need for carbohydrate and the reversibility of vernalization is, of course, not known yet. However, the metabolism which accompanies vernalization may well be worth analysis. Indeed, the way may have been opened to such an analysis by the recent experiments of Purvis (*4*), which indicate that, during a period of starvation of the rye embryo, some materials necessary not only for vernalization but also for growth are metabolized away. Perhaps at this point our developing knowledge of the special nutritional requirements of young embryos in culture may be brought to bear. A very recent paper by Lang and Melchers (*3*), unfortunately received too late for inclusion in the text, brings the two ideas together in another way. Biennial *Hyoscyamus niger,* which flowers after vernalization only if kept in long days, can be devernalized if given 10 short days at 38°. This treatment must, however, be applied immediately (within four days) after the vernalization by cold. Thus, the flowering condition or substance is destroyed before it has had time to act. Another recent piece of evidence strongly suggestive of the former, or hormonal, view is supplied by Holdsworth and Nutman's (*2*) study of the flowering of *Orobanche.* This parasite evidently initiates flowers only when its host, red clover, does so; in other words, the receptors for the flowering "hormone," whose production depends on day-length, are not only the buds of the host but also those of the parasite. The formation and destruction of special substances or, alternatively, the balance between their production and its inhibition is, of course, the general line of interpretation adopted by the workers in photoperiodism. The former of the two alternatives is essentially that of Hamner and of Borthwick, Parker, and their co-workers at Beltsville; the latter, that of Melchers and his collaborators. It is needless to add, however, that the nature of these hypothetical substances and the metabolic conditions under which they are produced remain completely unknown. Nevertheless, this vast hiatus does not at present interfere seriously with the development of the field, since these ideas are little more than interpretations and are not specifically formulated theories which can stand or fall by experiments designed to test them.

Another group of questions which we are perhaps not yet ready to formulate concerns the mode of action of the stimulus (or the substances). In the case of vernalization of the grasses the impetus to flower formation seems to appear as a change in the primary meristem; in the dicotyledons the contribution of Roberts and Struckmeyer suggests that it may be the secondary meristem which shows the initial and determining responses. If it be the meristems which are initially changed, then the subsequent reactions leading to flowering may result from differences in the supply system and therefore in the materials made available to the developing initials. Similar effects exerted through the transporting system may be operative in the thermoperiodic phenomena described by Went.

Some of the questions are less broad and are susceptible of immediate attack. One of these is the nature of the photo-receptor pigment, the measurement of whose absorption spectrum by the Beltsville group is described in one of the chapters of this volume. Another is the role of sugar-feeding and induced fermentation studied by Melchers, Lang, and Claes and discussed in the articles by Murneek and Hamner. Still another is the relation of auxin production to flowering; it is a striking fact that, in pineapple, auxin greatly hastens flowering, while in other plants its effect tends to be in the opposite direction. Indeed, Galston (*1*) has ascribed the effect of triiodobenzoic acid in increasing the number of flower-buds in soybeans to the antagonistic effect of

this substance on the auxin of the plant. The reduction of cambial activity preceding flowering in the plants studied by Roberts and Struckmeyer would also indicate an opposition between auxin and flowering. The very rapid reactions to change in day-length in such plants as the soybean, of course, would not suggest that such cambial changes were causative in themselves, but they could certainly be an indication of decreased auxin production. Very recently, both Thurlow and Bonner (*7*) and Leopold (unpublished data) have found, using different plants and different methods, that auxin, applied externally, may inhibit to some extent the normal process of flowering. A number of older observations, both botanical and horticultural, point in the same direction, while the peculiar and (at present) isolated case of pineapple, whose flowering is promoted by auxin, cannot be overlooked. Whether auxin (either as a promoter or an inhibitor) plays a major role in the flowering process, however, is far from established, though there is doubtless an interesting avenue here to be opened up. A more extensive discussion of this phase of the problem has been given elsewhere (*6*).

It may be—and this is undoubtedly the usual course of research—that further study of these more concrete problems will lead to a gradual elucidation of the broader and more intangible unknowns. But, as was stated at the outset, the state of the field is such that a single clear-cut result might change its whole aspect almost overnight.

The consequences of major progress in this area are very great, not only for pure science but for agriculture. In these days when so much of the world is near to starvation no worker can fail to carry this thought in the back of his mind, in spite of the frequent statement that research is its own reward and that no further incentive is necessary. One purpose of a symposium like the present publication is to enable the individual student to effect something of a synthesis in his views. Such a synthesis can hardly fail to engender new ideas and thus to quicken the pace of progress.

References

1. Galston, A. W. *Amer. J. Bot.*, 1947, **34**, 356–360.
2. Holdsworth, H., and Nutman, P. S. *Nature, Lond.*, 1947, **160**, 223.
3. Lang, A., and Melchers, G. *Z. Naturforsch.*, 1947, **2b**, 444–449 (received May 1948).
4. Purvis, O. N. *Ann. Bot. N. S.*, 1947, **11**, 269–283.
5. Sen, B., and Chakravarti, S. C. *Nature, Lond.*, 1946, **157**, 266; 1947, **159**, 783–784.
6. Thimann, K. V. In *The hormones; chemistry, physiology and applications.* New York: Academic Press, 1948. Chap. 3.
7. Thurlow, J., and Bonner, J. *Amer. J. Bot.*, 1947, **34**, 603. (Abstract.)
8. Whyte, R. O. *Crop production and environment.* London: Faber & Faber, 1946; See also: David, R. *Facteurs de développement et printanisation des végétaux cultivés.* Paris: Hermann et Cie, 1946.

TECHNICAL PAPERS

Mechanical Transmission of a Virus Disease to Cucumber From Sour Cherry

J. Duain Moore, J. S. Boyle, and G. W. Keitt

Department of Plant Pathology, University of Wisconsin

Investigations of yellows and necrotic ring spot, virus diseases of sour cherry (*Prunus cerasus* L.), have been sharply limited because the only known mode of transmission of these diseases has been by grafting, and the known host range has been limited to stone fruits (*1–4*). Since mechanical transmission to herbaceous plants would open many possible avenues of investigation, experiments with this objective were undertaken.

In greenhouse studies in the spring of 1947 it was found possible to transmit mechanically a virus disease to cucumber (*Cucumis sativus* L. variety Ohio) from sour cherry (variety Montmorency). This was accomplished by grinding very young cherry leaves that were just beginning to show the initial symptoms of necrotic ring spot and by rubbing, with carborundum dust as an abrasive, the undiluted expressed juice on the cotyledons of young cucumber plants. While the percentage transmission in any single inoculation experiment was low, transmission was accomplished from 8 cherry trees known to be affected by both necrotic ring spot (*2*) and yellows (*3*) and from one known to be affected by necrotic ring spot but not by yellows. Similar tests of 8 cherry trees free from necrotic ring spot and yellows gave no symptoms on cucumber. Adequate numbers of uninoculated control cucumber plants remained, without exception, free of virus symptoms. Similar attempts to transmit disease from older cherry leaves have been unsuccessful. Mechanical transmission from cucumber to cucumber was obtained readily.

There has been some variation in symptoms on the cucumber with different temperatures, ages of the cucum-

ber plants at the time of inoculation, and cucumber varieties. However, the following symptoms were commonly expressed after inoculation on the cotyledons of young cucumber plants on which the primary leaf was just beginning to unfold and when the plants were kept in an air-temperature range of 20–28° C: From 2 to 4 days after inoculation, small, round, yellow rings appeared on the cotyledons. These rings soon became yellow blotches that coalesced to form a marked mottle. The cotyledons usually persisted as turgid functional organs for many weeks, in contrast to those of normal plants, which soon became functionless, turned brown, and withered. Within 24–48 hrs after symptoms developed on the cotyledons, yellow spots began to appear on the unfolding leaves, beginning at the base of the leaf. The spot symptoms usually were followed by the development of yellow rings, mottle, and crinkle of the affected leaves. Occasionally the primary leaves wilted and died. The apical growing point was killed very quickly, and numerous plants have been maintained for several weeks with only the two cotyledons and the primary leaf. About 30–45 days after inoculation, bud proliferation, without elongation, was apparent in the axis of the killed growing point. Many flowers and dwarfed leaves developed in a very compact rosette. In a few instances, after a prolonged period of high greenhouse temperatures, several of these badly rosetted plants developed weak, spindly shoots.

A limited number of inoculations from cucumber to cherry were made in the greenhouse late in the season of 1948 by placing small pieces of cucumber leaf under the bark of cherry trees. Definite symptoms of necrotic ring spot developed on leaves of one of 6 cherry trees so inoculated. The diseased cucumber plant in this case had been inoculated from a cherry tree known to be affected by both necrotic ring spot and yellows. Ring spot symptoms appeared on one of 3 cherry trees similarly inoculated at the same time with leaf tissue from sour cherry showing necrotic ring spot, and the 3 uninoculated control trees showed no symptoms. The conditions of these experiments were evidently marginal for transmission of necrotic ring spot.

Final conclusions regarding the identity of the virus (or possibly viruses) that incites the disease on cucumber have not yet been reached. The symptoms on cucumber, the single case of transmission from a cherry tree known to be affected by necrotic ring spot but not by yellows, and the single case of apparent transmission of necrotic ring spot from cucumber to sour cherry strongly suggest that the necrotic ring spot virus incites the cucumber disease. However, the possibility is not excluded that another virus (or viruses) from sour cherry may be involved. Since the period of incubation for cherry yellows is long, the cherry trees inoculated from cucumber cannot be read for possible yellows symptoms until 1949. Further work on the identity of the virus (or viruses) that incites the cucumber disease is now in progress.

This, so far as we know, is the first mechanical transmission of a stone fruit virus disease and the first transmission of a virus disease from sour cherry to an herbaceous host.

References

1. Berkeley, G. H., and Willison, R. S. *Phytopath.*, 1948, **38**, 509–518.
2. Hildebrand, E. M., Berkeley, G. H., and Cation, D. *Handbook of virus diseases of stone fruits in North America* (Mich. agric. exp. Sta. Misc. Publ.), 1942.
3. Keitt, G. W., and Clayton, C. N. *Phytopath.*, 1943, **33**, 449–468.
4. Moore, J. Duain, and Keitt, G. W. *Phytopath.*, 1944, **34**, 1009. (Abstract.)

Crystallization of Hypophyseal Growth Hormone[1]

Choh Hao Li, Herbert M. Evans, and Miriam E. Simpson

Institute of Experimental Biology, University of California, Berkeley

Some time ago we described a method (*2*, *3*) for the preparation of the anterior hypophyseal growth hormone in pure form from ox pituitaries. Although it was not

Fig. 1. Crystalline hypophyseal growth hormone (×125).

a crystalline preparation, physicochemical and biological studies then and since have indicated that it is a pure protein. Recently Fishman, Wilhelmi, and Russell (*1*) reported that a crystalline pituitary protein with high growth activity may be obtained by alcohol fractiona-

[1] Aided by grants from the American Cancer Society (through the National Research Council, Committee on Growth), the U. S. Public Health Service (RG-409), and the Research Board of the University of California, Berkeley.

ion; the crystalline preparations consisted of two components as revealed by electrophoretic analysis. In this communication we wish to report the crystallization of growth hormone from our pure amorphous material by a technique similar to that of Fishman, *et al.*

Approximately 0.1% of the pure growth-hormone solution was adjusted to pH 10 with calcium hydroxide solution and brought to an alcohol concentration of 10% by a slow addition of 1:1 alcohol-water at 2° C. A small amount of the hormone was precipitated out and removed by centrifugation. The supernatant usually has a pH 9.5; if not, it was adjusted to this pH with 0.1 N HCl. Alcohol-water (1:1) was again added very slowly until the alcohol concentration was 15%. On standing at 2° C, crystals appeared as thin plates (Fig. 1). The crystals were highly soluble at room temperature and disappeared quickly during microscopic examination. To obtain a satisfactory crop of crystals, the protein concentration must be low, and the temperature should be below or at 2° C.

When crystalline preparations were assayed by the body growth or tibia test on hypophysectomized rats, there appeared no difference in their activity as compared with that of the starting material, indicating that further concentration or "fractionation" had not been achieved by crystallization. Electrophoretic analysis of the crystals gave results identical with those obtained with the amorphous pure preparation.

References

1. Fishman, J. B., Wilhelmi, A. E., and Russell, J. A. *Science*, 1947, **106**, 402.
2. Li, C. H., and Evans, H. M. *Science*, 1944, **99**, 183.
3. Li, C. H., Evans, H. M., and Simpson, M. E. *J. biol. Chem.*, 1945, **159**, 353.

Six-Segment Head Regenerates in an Earthworm, *Eisenia foetida* (Savigny) 1826[1]

Esther Carpenter[2]

Smith College, Northampton, Massachusetts

In heads regenerated by *E. foetida* after excision of 6 or more segments there are at most, according to Morgan (*4*), only 4 or 5 segments. A similar limitation of segment number in head regenerates (*1*) has been assumed to be characteristic of *E. foetida* and other earthworms of the same family. There are in the literature, however, at least two records of greater numbers of segments in head regenerates of this species. Morgan (*3*) included in tables two 6-segment head regenerates observed 4 and 6 months after operation. In one, the 12 anterior segments had been excised. The number of segments removed from the other was not counted at the time of operation but was estimated later to be 10(½). In 1898 Michel (*2*) reported one head regenerate of 6 segments after the removal of 8 and one of 7 after the removal of 7. Both were obtained in less than 4 weeks.

In the present study 30 specimens of *E. foetida* from Virginia were operated on in January and February. All were clitellate animals. The presence of male pores on segment xv and the clitellum in normal position were ascertained (*5*). Worms were anesthetized in dilute chloretone and the 10 anterior segments amputated with a razor blade exactly at intersegmental furrow 10/11. Animals were examined daily at first and then twice a week. Specimens were fixed after 4–8 weeks.

Twenty-one animals survived the operation, and each regenerated a head. The number of segments in the 10 normal head regenerates was as follows: 4 in 2 specimens; 5 in 5 specimens; and 6 in 3 specimens. The 11 remaining worms had head regenerates of 3–5 normal segments plus one or more partial segments.

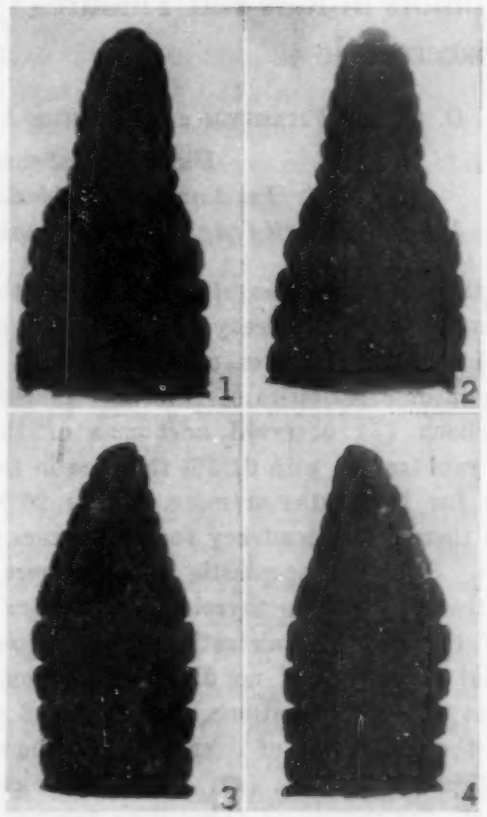


Fig. 1. (1 and 2) Dorsal and ventral views of the same 6-segment head regenerate. (3) Lateral surface view of another 6-segment head regenerate. An additional furrow shallower than the others can be seen in the proximal part of segment ii. (4) Same specimen as (3) but with the focus at the median plane. All specimens were in Cellosolve and photographed × 17.

Among the 10 normal head regenerates, three exceptions were found to the generally accepted statement concerning head regeneration in *E. foetida*. These are the first 6-segment head regenerates to be recorded for this species after amputation exactly at intersegmental furrow 10/11. Dorsal and ventral views of one of these are shown in Fig. 1 (1 and 2). Another specimen, cut through the median plane and photographed in Cellosolve, is shown in Fig. 1 (3 and 4). Segment ii (3) has

[1] Contributions from the Department of Zoology, No. 219.

[2] The author is indebted to Dr. G. E. Gates, of the Museum of Comparative Zoology, Harvard University, for many helpful suggestions and for access to manuscripts not yet published.

an additional lightly marked furrow toward its proximal boundary.

The 11 head regenerates considered, for the present, to be abnormal fall into two classes: those which are asymmetrical, perhaps because of some environmental factor such as temperature and those which have additional furrows symmetrically demarcated ventrally, or ventrally and laterally. Those in the second group and the condition indicated in segment ii (3) could be interpreted as indicating the possibility that additional segments may be added to the head regenerate later.

References

1. Hyman, L. H. *Amer. Nat.*, 1940, **74**, 513–527.
2. Michel, A. *Bull. Sci. France et Belgique*, 1898, **31**, 245–420.
3. Morgan, T. H. *Quart. J. Mic. Sci.*, 1895, **37**, 445–459.
4. Morgan, T. H. *Columbia U. Biol. Ser.*, 1901, **VII**, 9.
5. Smith, Frank. *Proc. U. S. Nat. Mus.*, 1917, **52**, 157–182.

Liver Tumors in Rats Fed Thiourea or Thioacetamide

O. Garth Fitzhugh and Arthur A. Nelson

Division of Pharmacology,
Food and Drug Administration,
Federal Security Agency, Washington, D. C.

The striking effectiveness of thiourea and thioacetamide in preventing orange decay (*1–3*) and the occurrence of the thiourea in the juice of treated fruit led us to study the chronic toxicities of these substances. Purves and Griesbach (*5*) observed adenomas of the thyroid glands in rats treated with 0.25% thiourea in their drinking water for 12 months or more. After 20 months of treatment there was a tendency for the tumors to become malignant. Since no neoplastic changes were observed in other tissues than the thyroid glands after this long period of thiourea administration, these observers concluded that thiourea had no direct carcinogenic action. In contrast to the observations of Purves and Griesbach, we found the production of liver tumors to be one of the chronic effects of thiourea (*4*). The present communication reports the nature of these liver tumors and their high incidence in thiourea-fed rats.

In a two-year chronic toxicity study albino rats, 21 days old, 18 to a group, were fed thiourea at levels of 1, 0.5, 0.25, 0.1, 0.05, 0.025, and 0.01% in a diet of ground commercial rat biscuits. Control animals received the basic diet. All animals were permitted unrestricted access to both food and water.

At dosage levels of 0.25% or more thiourea, the outstanding gross lesion was enlargement of the thyroid gland. The thyroid enlargement was marked at the 1.0% level and decreased with decreasing dosage, but was distinct at 0.25% thiourea. The thyroid weights of the animals on dosage levels of 0.05% or lower were not significantly different from those of the controls. Thiourea at dosage levels of 0.25% or more stunted the growth of the rats. This effect was marked during the fast-growing period of the first three months on the experimental diet. When the rats on these higher dosage levels became adult, they were short, chubby, and very fat. They appeared listless and, when disturbed, made no effort to move around in their cages. All animals at the dosage levels of 0.25% or more thiourea died within the first 17 months of the experiment. Lower dosages had no effect on mortality.

The liver showed marked gross changes, especially in the surviving animals, at dosage levels of 0.10% and below. At levels of 1.0 and 0.5% the liver and, to a lesser extent, the viscera in general were in the majority of instances moderately pale. The pallor was not so pronounced at 0.25% and was essentially absent below this level. In no animal was there an hepatic cirrhosis or even a roughness of the liver surface, except as caused by the presence of tumors.

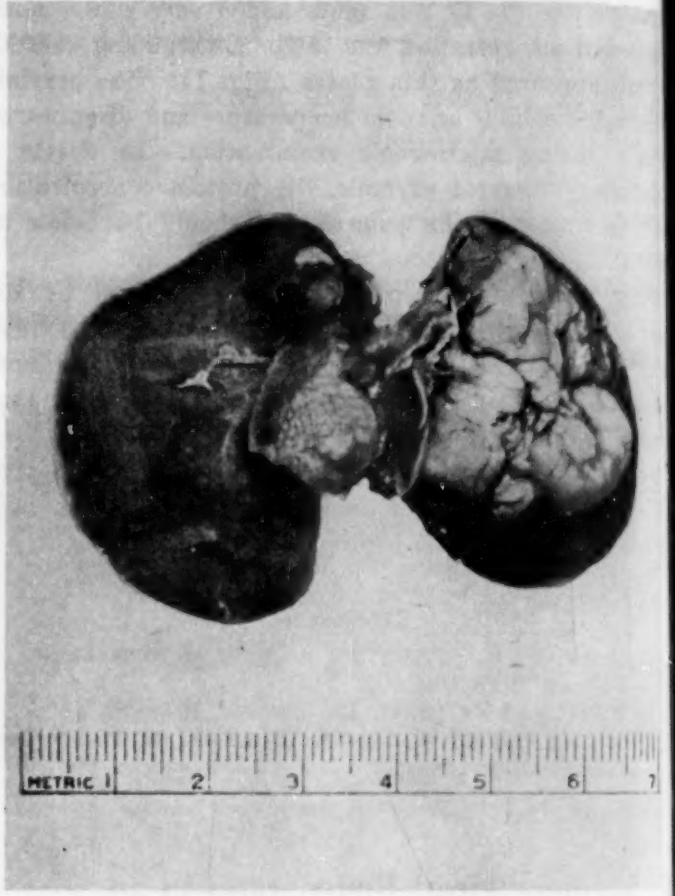


Fig. 1. Large liver tumor in rat fed 0.1% thiourea for two years.

Of the 29 experimental rats surviving the two-year feeding period, 14 showed liver tumors. There was a general correspondence between dosage level and tumor size and incidence. Only one of the nonsurviving treated rats, and none of the 18 controls, showed such a tumor. For comparison, the general run of our rats, whether controls or those fed a variety of added substances in their diets and surviving a two-year experimental period, show approximately a 1% incidence of spontaneous hepatic tumors of the type described below. In the livers of the animals with these spontaneous tumors, also, cirrhosis is absent. The significance, therefore, of an almost 50% tumor incidence in the surviving thiourea-fed animals becomes apparent.

In size, 4 of the 15 liver tumors were 2.5 × 2.5 × 2.0 cm or larger, up to 4.0 × 3.5 × 2.5 cm. One of the larger ones is illustrated in the photograph (Fig. 1). The rest varied from this size down to 4 mm in diameter. In about half of the instances there were, in addition to the main tumor, one or a few smaller nodules, some of which had a distinct tumorous appearance while others were not grossly typical. The tumors were on the whole very similar to each other in appearance, being well circumscribed and sharply demarcated from the surrounding liver because of their lighter color. This was especially true for the larger ones. There was no fibrous encapsulation. All sites in the liver were equally affected.

Microscopic hyperplasia of the thyroid gland paralleled the gross enlargement in a general way, but at any given dosage level was more consistent. At the 1.0% level the hyperplasia averaged marked in degree, at 0.5% moderate to marked, at 0.25% moderate, at 0.10 and 0.05% very slight; at levels below this there was little, if any, hyperplasia. No detailed histologic description of the thyroid hyperplasia seems necessary, since it was essentially identical with that reported by various authors.

The liver showed as its most consistent lesion a mild generalized hypertrophy of the hepatic cells. Accompanying this were slight irregularity of the hepatic architecture, slight (in rare instance, moderate) bile duct proliferation, and minimal degrees of fatty change (as evidenced by vacuolation in the paraffin sections) and hyaline appearance of the hepatic cell cytoplasm. No portal fibrosis was evident. A peculiarity of these hepatic changes was the fact that at any given dosage level there was very little progression or increase in degree between the earliest animals examined and the latest. There was, however, a gradual reduction in degree as the dosage level was decreased, and at 0.05% and below these hepatic alterations were either minimal or absent, except in the near vicinity of some tumors.

The liver tumors were quite uniform in their histology and, except for minor areas of variation, were composed of irregular cords of cells resembling the surrounding hepatic cells. In the smaller tumors the resemblance was rather close, while, as the tumors became larger, their cells also became larger and less typical. The nuclei and nucleoli showed a slight relative prominence as compared to the nonneoplastic hepatic cells. Mitoses were rarely seen. Normal hepatic lobulation was lost even in the smallest tumors. Endothelial-lined sinusoids were generally present between the cell cords, but, as the tumors became larger, the sinusoids became more irregular in size and shape. Generally the tumor borders were sharply demarcated from the nonneoplastic hepatic cells, but there was little or no fibrous encapsulation. Generally the neoplastic masses had an expansive appearance and pushed aside and compressed the adjacent liver. Features present in the tumors in small amount or in slight degree were focal bile duct proliferation, fibrosis, focal necrosis, solid masses of tumor cells, and telangiectasia. With full realization of the difficulties of the nomenclature of hepatic cell masses, we can only say in the limited space available that we consider these tumors as hepatic cell adenomas.

Apart from the thyroid and liver, certain other structures showed changes attributable to the feeding of thiourea and not simply nonspecific accompaniments of inanition. In the spleen and adrenal, these changes were rarely seen at levels of 0.10% and below, but above this level they were nearly consistent, although somewhat less pronounced at 0.25% than at 1.0%. The splenic pulp was markedly atrophic, the follicles less so, and in contradistinction to the usual atrophic spleen the pulp was markedly congested and contained a slight to moderate excess of hemosiderin over the amount ordinarily seen. The reticular zone of the adrenal cortex was congested and atrophic. In the kidney, one-third of the animals at 0.25%, increasing to two-thirds at 1.0%, showed small to moderate numbers of calcified tubular casts at the vicinity of the corticomedullary junction; several of these kidneys also contained small amounts of calcified debris in the pelvis. Reduction or cessation of spermatogenesis, reduction of bone growth at the epiphyseal lines, and hypoplasia of the bone marrow could all be accounted for by the degree of bodily stunting present, but a slight to moderate thickening of the cancellous bone trabeculae in some of the higher-dosage animals could not be so accounted for.

Lung, heart, pancreas, stomach, small intestine, colon, uterus, ovary, parathyroid, lymph nodes, thymus, and voluntary muscles all showed no changes specifically attributable to thiourea.

In a chronic toxicity study similar to that for thiourea, 50 rats, 10 to each group, were fed thioacetamide at levels of 0.1, 0.05, 0.025, 0.01, and 0.005%. At dosage levels of 0.025% and above there was a marked effect on survival time and a significant effect on growth rate. The outstanding lesion was a cirrhosis of the liver. At 0.1% thioacetamide, survival was for less than a month, and there was no gross hepatic cirrhosis; however, the liver of the rats at this level showed microscopically a complicated pattern of damage, two features of which were a moderate degree of bile duct proliferation and a relatively enormous increase in size of the hepatic cell nucleoli. At 0.05% a marked degree of coarsely nodular cirrhosis of the liver was present after the first few weeks, and one of the livers contained a 3.5-cm area of histologically malignant tumor originating from hepatic cells. Such a tumor has never occurred spontaneously in our rats. At 0.025% cirrhosis was slight to moderate in degree, and there were no liver tumors. At 0.01 and at 0.005% there was minimal or no cirrhosis, but 1 of the 6 surviving animals had a 1-cm hepatic cell adenoma. Thyroid, lung, heart, spleen, pancreas, gastrointestinal tract, kidney, adrenal, lymph nodes, gonads, bone marrow, bone, muscle, and parathyroid showed either no changes attributable to treatment or, if there were any, they were so slight as to be questionable.

It is concluded that thiourea, administered orally to albino rats for a prolonged period of time, induces liver tumors, without liver cirrhosis, in a large percentage of

cases at concentrations which may be below those producing hyperplasia of the thyroid gland. Thioacetamide appears to be slightly tumorigenic in the rat liver and, in addition, is a very potent producer of nodular cirrhosis.

References

1. CHILDS, J. F. L., and SIEGLER, E. A. *Phytopath.*, 1944, **34**, 983.
2. CHILDS, J. F. L., and SIEGLER, E. A. *Science*, 1945, **102**, 68.
3. CHILDS, J. F. L., and SIEGLER, E. A. *Ind. eng. Chem.*, 1946, **38**, 82.
4. FITZHUGH, O. G., NELSON, A. A., and HOLLAND, O. L. *Fed. Proc.*, 1948, **7**, 218.
5. PURVES, H. D., and GRIESBACH, W. E. *Brit. J. exp. Path.*, 1947, **28**, 46.

Desoxypentosenuclease in Yeast and Specific Nature of Its Cellular Regulation[1]

STEPHEN ZAMENHOF and ERWIN CHARGAFF

Department of Biochemistry,
College of Physicians and Surgeons,
Columbia University, New York City

Evidence has been obtained in this laboratory of the occurrence in yeast (*Saccharomyces cerevisiae*) of two agents concerned with desoxypentose nucleic acids (DNA), viz., a depolymerase (DNase) and an inhibitor of DNase having interesting specific properties.

When yeast is ground mechanically and the layer of cell debris treated with M NaCl solution, the extract, as was shown recently (*1*), includes a highly polymerized DNA. The same extract has now been found also to contain a DNase in a largely inhibited state, from which it is slowly released on storage at 4°. The increase in activity is about 50-fold within 3 months. Extracts of the ground cells with distilled water contain free inhibitor but no enzyme.

Washed yeast was crushed, distilled water being used as suspending fluid, and the debris extracted with M NaCl, as described previously (*1*). The viscous mixture (500 cc) was kept in the refrigerator for 1–4 months, clarified by centrifugation at 4,000 rpm, dialyzed, and dried from the frozen state in a vacuum. The solution of the residue in 30 cc of water was centrifuged at 20,000 rpm and the supernatant brought to 0.6 saturation with solid ammonium sulfate. The solution of the precipitate, collected at 20,000 rpm, was subjected to a rocking dialysis against ice-cold distilled water for 7 hrs and again centrifuged at high speed. The sediment was washed with water and then extracted with 30 cc and again with 12 cc of M NaCl. The combined extracts, clarified by centrifugation at 20,000 rpm, were dialyzed and evaporated in a vacuum in the frozen state. The DNase preparation weighed 27 mg. Even high dilutions of this agent produced a rapid drop in viscosity of solutions of thymus DNA and of yeast DNA (*1*). It had an activity of about 1,200 units/mg of protein, as defined by McCarty (*4*). In a concentration of 0.6 mg/cc it was free of proteolytic (*5*), nucleotidase, and ribonuclease activities.

Yeast DNase resembled the desoxyribonuclease of pancreas (*3*, *4*) in requiring Mg ion for activation and in being labile to heat; the activity was destroyed completely by heating to 55° for 15 min. It differed, however, from the pancreatic desoxyribonuclease in several important respects. It was insoluble in water but soluble in salt solutions. Its activity optimum lay below pH 6.2; at pH 8.1 only 20% of its activity was retained. The most significant difference consisted in its being specifically inhibited by a yeast fraction which, however, had no inhibiting effect on purified pancreas desoxyribonuclease and on crude DNase preparations from *Neurospora crassa*, germinating barley, and calf thymus, which will be discussed on a later occasion.

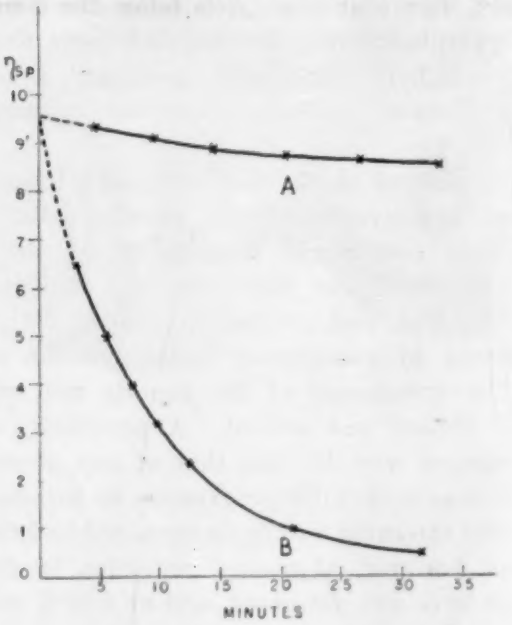


FIG. 1. The specific viscosities of mixtures of thymus DNA (sodium salt) and yeast DNase with (A) and without (B) DNase inhibitor are plotted as the ordinate. The abscissa indicates the duration of incubation of the mixtures before testing, at 30°. Mixture A contained 1.7 mg of DNA, 3 micromoles of Mg, 2.5 units of yeast DNase, and 2.2 mg of inhibitor/cc of veronal buffer of pH 6.6. In mixture B the inhibitor was omitted.

The DNase inhibitor, present in aqueous and salt extracts of ground yeast cells, caused up to 94% inhibition of yeast DNase. A typical experiment is reproduced in Fig. 1. The inhibitor appears to be a water-soluble labile protein, its activity being destroyed in less than 5 min at 55°. It is inactivated by crystalline trypsin, by ficin, and by a proteolytic enzyme preparation from crushed yeast. To the presence of the latter in the inhibitor preparations their inactivation on storage for 8–20 hrs at 30° or for 2–4 weeks at 4° probably is attributable. The inhibitor can be partially purified by precipitation at 0.8 saturation with ammonium sulfate.

[1] This work has been supported by a research grant from the U. S. Public Health Service.

[2] We are very grateful to Dr. M. McCarty for a specimen of this preparation.

Preliminary experiments on the mechanism of this inhibition reaction, which is instantaneous, suggest that it is reversible and noncompetitive. Indications have been obtained that *Saccharomyces carlsbergensis* likewise contains a DNase inhibitor which, however, appears to behave somewhat differently.

A full account of this and related work on other cellular systems, including those of higher organisms, will appear at a later date. But attention may be drawn to the following sequence of autolytic reactions, possibly delicately balanced in the living cell: (1) activation of yeast protease (*2*); (2) digestion of DNase inhibitor; (3) liberation of active DNase; (4) depolymerization of DNA. If, as appears likely, the cleavage of the DNA macromolecules is of importance in the life of the cell, the evidence of the existence within the cell of a specific regulation of this process may be of more general biological interest.

References

1. CHARGAFF, E., and ZAMENHOF, S. *J. biol. Chem.*, 1948, **173**, 327.
2. GRASSMANN, W., and DYCKERHOFF, H. *Z. physiol. Chem.*, 1928, **179**, 41.
3. KUNITZ, M. *Science*, 1948, **108**, 19.
4. MCCARTY, M. *J. gen. Physiol.*, 1946, **29**, 123.
5. NORTHROP, J. H., and HUSSEY, R. G. *J. gen. Physiol.*, 1923, **5**, 353.

Effect of Flavonoids (Vitamin P) on Mortality From Total Body Roentgen Irradiation[1]

WILLIAM G. CLARK, REX P. UNCAPHER, and MARY L. JORDAN

Scripps Metabolic Clinic and *Scripps Memorial Hospital, La Jolla, California*

In previous papers Clark and Geissman (*1, 2*) reported a test for flavonoids and related compounds (vitamin P-like substances) based on the potentiation of the epinephrine response of isolated mammalian smooth muscle. In a study of the relation of molecular structure to activity, some 70 pure compounds were examined, and the minimum structure essential for high activity was predicted, synthesized, tested, and found to confirm the prediction.

In attempts to extend these and other observations to the intact animal, among other things a study was included of the effects of these compounds on the hemorrhagic syndrome associated with total-body roentgen irradiation. This study was initiated in September 1947, and the purpose of the present communication is to demonstrate the potential usefulness of this approach in further experimental assessment of the antihemorrhagic effects of the flavonoid pigments.

Griffith, *et al.* were the first to demonstrate a beneficial effect of flavonoids in experimental roentgen-irradiation injury. They found a beneficial effect of rutin[2] therapy in accelerating the restorative processes following severe X-ray burns of rats' extremities (*8*) and in preventing the capillary fragility increase following intraperitoneal administration of radon ointment in rats (*7*). They also indicated that rutin probably had no beneficial effect in total-body roentgen-irradiated rats but gave no particulars (*7*).

Rekers and Field (*10*) later reported a decrease in mortality of dogs by rutin therapy before and after 350 r total-body roentgen irradiation.

The beneficial effect of rutin in the case of the X-ray burns of rats' extremities was limited to an acceleration of the restorative processes, since there was no effect on the time of onset or the severity of the lesions. This probably is related to the similar beneficial effect of rutin in the prevention of tissue loss in frostbite gangrene in rabbits' extremities, reported by Fuhrman and Crismon (*4, 5*).

We wish to report the effect of one of several flavonoid substances being studied in several species (rats, mice, guinea pigs) of small laboratory animals subjected to approximately median lethal doses of total-body roentgen irradiation.

Large, healthy guinea pigs of approximately 500-gm body weight were fed on Rockland guinea pig ration[3] and given supplementary ascorbic acid in 0.2% concentration fresh daily in the drinking fluid. One group served as controls and the other as flavonoid treated, for which the drinking water also contained 0.2% "calcium flavonate,"[4] prepared fresh daily. Previous experiments had indicated that single, daily, oral, large doses of flavonoids are not as effective as constant ingestion in the food or water.

After a week of such treatment the animals were given 220–225 r total-body irradiation[5] in a single dose, not including backscatter. They were placed in a multicompartment wooden box, controls and experimentals being arranged alternately in a checkerboard fashion, 4

[1] Supported by a grant from the U. S. Public Health Service. Grateful acknowledgment is made of the suggestions and encouragement of Eaton MacKay, in whose laboratories this work was done.

[2] Quercetin-3-rhamnoglucoside, a common flavonoid active in decreasing capillary fragility, as first shown by Sevin (*11*) and later by Griffith, Couch, and Lindauer (*9*).

[3] Arcady Farms Milling Company, Chicago, Illinois.

[4] A water-soluble preparation from lemon peel, essentially free of water, sugars, and hesperidin. The alcohol extract of the fresh peels is precipitated in alkaline medium with calcium, the precipitate suspended in water and adjusted to an acid pH, reprecipitated by the addition of alcohol, filtered, and the material obtained from the filtrate by evaporation. It gives a cyanidin test about half as intense as rutin on a weight basis. Prepared and supplied by the California Fruit Growers Exchange, Sunkist Building, Los Angeles, California.

[5] GE Model KX-3, 220-kv deep therapy unit. The factors were: 200 kv, 20 MA, ½ mm Cu + 1 mm Al added filtration (HVL, 1.05 mm Cu), 100-cm target distance, 8.5 r/min. The unit is calibrated semiannually by a registered X-ray physicist. The variation in output over the past year has been less than 3%.

controls and 4 experimentals in each exposure, in a manner described by Goldfeder, *et al.* (*6*) for mice and with backscatter made uniform by use of a rice phantom, in accordance with the technique of Ellinger (*3*).

Following irradiation, treatment was continued for the duration of the experiment. Animals dying were autopsied. Clinical symptoms were graded twice weekly with emphasis on visible manifestations of anemia and purpura. Albinism lent itself best for the assessment of such symptoms.

In several experiments involving a total of 230 animals it was observed that, under the conditions described, 220–225 r consistently killed 67% of the animals, with 50% dead within 13 days. With the exception of occasional secondary infections, recovery from radiation injury usually was complete within 30 days; hence the experiments were terminated, although the animals remained under observation for several weeks thereafter.

The data in Table 1 illustrate the effect of "calcium flavonate."

TABLE 1

	Total No. guinea pigs used	Total No. died	Died %	50% death time (days)
Controls	45	30	67	13
Treated	26	9	35	..

The hemorrhagic symptoms (petechial hemorrhages, ecchymoses, generalized purpura) of the treated animals were considerably less marked than those of the controls.

It is concluded that under the experimental conditions described, a flavonoid preparation derived from lemons, administered in the drinking water, reduces the mortality from total-body roentgen irradiation by about half. In our opinion this justifies the employment of smaller laboratory animals than the dog in further studies of this nature and may offer an intact animal assay for vitamin P-like substances. Studies are in progress in attempts to elucidate the molecular configurations necessary for higher activity of the flavonoids and related substances by this and similar techniques.

References

1. Clark, W. G., and Geissman, T. A. *Fed. Proc.*, 1948, **7**, 21.
2. Clark, W. G., and Geissman, T. A. (To be published.)
3. Ellinger, F. *Radiology*, 1945, **44**, 125.
4. Fuhrman, F. A. *Fed. Proc.*, 1948, **7**, 38.
5. Fuhrman, F. A., and Crismon, J. M. *J. clin. Invest.*, 1948, **27**, 364.
6. Goldfeder, A., Cohen, L., Miller, C., and Singer, M. *Proc. Soc. exp. Biol. Med.*, 1948, **67**, 272.
7. Griffith, J. Q., Jr. *Proc. Inst. Med., Chicago*, 1947, **16**, 434.
8. Griffith, J. Q., Jr., Anthony, E., Pendergrass, E. P., and Perryman, R. *Proc. Soc. exp. Biol. Med.*, 1947, **64**, 322.
9. Griffith, J. Q., Jr., Couch, J. F., and Lindauer, M. A. *Proc. Soc. exp. Biol. Med.*, 1944, **55**, 228.
10. Rekers, P. E., and Field, J. B. *Science*, 1948, **107**, 16.
11. Sevin, A. *C. R. Acad. Sci.*, 1943, **216**, 505.

Urinary Flow, Excretion of Solutes, and Osmotic Work During Diuresis of Solute Loading in Hydropenia in Man

S. Rapoport, William A. Brodsky,[1] Clark D. West, and Bruce Mackler

Children's Hospital Research Foundation and *Department of Pediatrics, University of Cincinnati College of Medicine*

Interest in the study of the osmotic limitations of the kidney has been renewed in the last years after having lapsed since the early studies by Korányi and others (*5*). Gamble, in studies of man during water deprivation (*4*), came to the conclusion that 1,400 milliosmols/liter represented the maximum urinary concentration attainable. Given this fixed maximum value, a minimal urinary volume could then be calculated from any solute load. Studies by McCance and co-workers (*6*) added the information that forced osmotic diuresis in hydropenia produced by urea, sodium chloride or bicarbonate, and potassium chloride increased urinary flow while decreasing the level of urinary osmolarity. The conclusion was reached that for the substances studied the total solute concentration rather than the level of any one solute determined the maximum osmolarity of the urine.

Another aspect of the osmotic relationships of the kidney concerns the work involved to produce the observed concentration differences between urine and plasma. The concept of renal osmotic work was first applied by Dresser (*2*), Galeotti (*3*), and Rhorer (*8*). Later a general thermodynamic treatment of the minimal work necessary for the production of urine was given by Borsook and Winegarden (*1*). Recently Newburgh (*7*) refocused attention on the application of the concept and presented a discussion of the clinical implications of concentration changes which tend to reduce the renal work.

The studies to be reported were undertaken in order to determine in a broad manner, by the use of loading substances of various kinds, the pattern of urinary flow and excretion of solutes under the condition of water restriction. Furthermore, it was hoped to find out whether under such conditions a biologic maximum of renal osmotic work existed and, if so, whether it was the same or different for varying solutes. Such a maximum of work, if extant, would represent a measure of over-all work capacity of the kidney, with possible physiological and clinical implications.

The subjects were boys, 8–15 years of age, with normal renal function and without major disease. One group of young diabetic patients was included for the study of forced diuresis produced by glucose. The loading substances were administered as a rule in amounts of 500–2,000 milliosmols/1.73 m^2 of body surface, by the oral or, more often, the intravenous route, in concentrated

[1] National Institute of Health Postdoctorate Research Fellow.

solution. The subjects were fasting and had received no water for 16 hrs previous to the experiment, and were excreting urine at rates of 0.5 ml/min or less (except the diabetic subjects). Eleven loading substances were studied: glucose, sucrose, mannitol, sorbitol, sorbose, xylose, urea, creatinine, sodium *p*-aminohippurate, sodium sulfate, and sodium chloride. In some experiments the entire course of diuresis, until the urine flow returned to preloading levels, was followed; in others chief emphasis was laid on observing the periods of maximum flow. Blood and urine were collected at appropriate intervals and were analyzed for the loading solute, as well as sodium, potassium, phosphorus, chloride, urea, and, in some instances, sulfate. On urine the freezing point was also determined, and the total osmolarity at infinite dilution calculated. The solutes determined accounted as a rule for 85 ± 10% of the total solutes in the preloading urine specimens and for as much as 90–95% of the total during diuresis. The loading solute (or two solutes in the case of salts) accounted usually for 60 ± 10% of the total. Fifteen subjects were studied in this manner over 111 periods of collection.

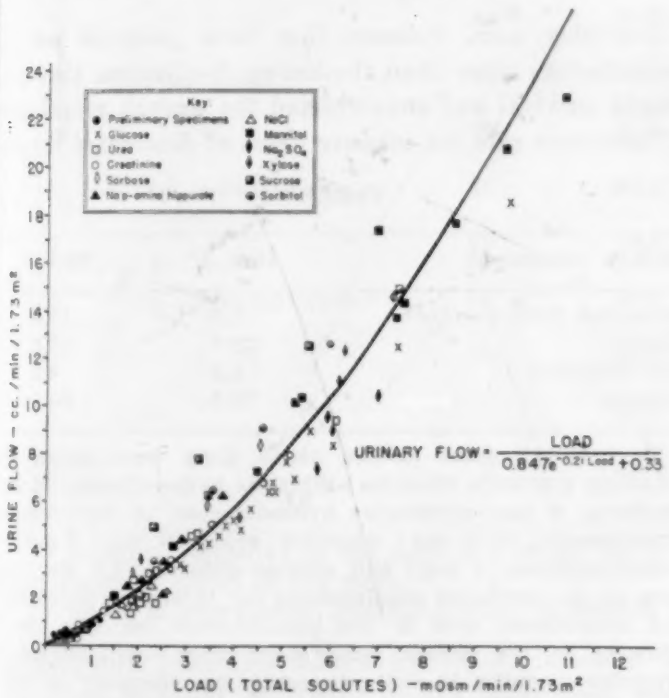


FIG. 1. Urine flow vs. solute excretion in man during hydropenia. Data on 111 periods, including those of minimal flow and those during diuresis forced by various loading substances, are included. The solid line drawn through the points represents the values calculated from the formula,

$$\text{Urinary flow} = \frac{\text{load}}{0.847e^{-0.21\ \text{load}} + 0.33}.$$

As may be seen from Fig. 1, a constant relationship prevailed between solute excretion and urine flow, regardless of the nature of the predominant solute in the urine. This relationship held over the observed range of urine flows from less than 0.5 ml to 24 ml/min/1.73 m². Considering the variety of substances studied, it is evident that the pattern of urinary flow is independent of the nature of urinary excretion, whether it be predominantly by filtration (mannitol, sucrose, xylose, sulfate) or filtration combined with tubular secretion (*p*-aminohippurate), or filtration combined with tubular reabsorption (urea, sodium chloride). A necessary conclusion is also that it is not the quantity of solutes in the glomerular filtrate, but only the amount finding its way into the urine, that determines the urinary flow. Consequently, the urinary flow is independent of the level of the clearance or of the plasma level of any solute. The dependence of urinary flow on solute load (U × V) alone led to the consideration of the form of this relation. The basic assumption that with increasing solute load the urinary concentration decreases asymptotically to the level of the plasma concentration may be expressed as

$$(1)\quad -\frac{\text{d conc.}}{\text{d load}} = k\ (\text{conc.} - B),$$

where k is a proportionality constant and B is the plasma concentration. Integration leads to the expression

$$(2)\quad -\ln(\text{conc.} - B) = k\ \text{load} + A,$$

where A is the integration constant and the other symbols have the same meaning as before. In exponential form and rearranged, the equation is

$$(3)\quad \text{conc.} = A'e^{-k\ \text{load}} + B.$$

Values for the constants A′ and k may be readily derived from equation 2, which is that of a straight line, with A, *i.e.* ln of A′, as the intercept and k as the slope. Choosing 0.33 osmols/liter as the value for B, and using the least squares method for calculating the best straight line, the values of 0.847 for A′ and 0.21 for k were obtained. The final equation is then

$$(4)\quad \text{conc.} = 0.847e^{-0.21\ \text{load}} + 0.33,$$

where urinary concentration is expressed in osmols/liter. From the identity load = concentration × flow, an equation for flow in terms of load may be obtained:

$$(5)\quad \text{urinary flow} = \frac{\text{load}}{A'e^{-k\ \text{load}} + B}.$$

The line drawn through the data of Fig. 1 indicates the calculated curve, which fits the observations for the entire range well.

Calculations of the renal osmotic work by the formula (*3*)

$$(6)\quad W = RT\ V\ (U \ln U/P + P - U),$$

where W indicates the work, R is the gas constant, T is the absolute temperature, U and P are the urinary and plasma concentrations, and V is the urinary flow, led to the conclusion that the kidneys were in a relatively resting state in the preloading periods, when minimal urine flow and maximal solute concentration prevailed. The amount of osmotic work could be increased about 10-fold by solute loading up to a maximum value of 4.2 ± 0.5 cal/min/1.73 m² of body surface, a value which could not be exceeded by increasing the load. An increase of

the amount of loading substance administered, while producing increasing urine flow, also resulted in higher plasma level of the solute so that the work remained constant. A maximum value in the same range was observed for the following solutes: glucose, sucrose, mannitol, xylose, sorbitol, creatinine, and sodium sulfate. Sorbose and *p*-aminohippurate were not used in sufficient amounts to produce adequate loads. Maximum work was not obtained with urea or sodium chloride.

From equation 2 it follows that under the conditions of hydropenia here considered, the U/P ratio is the main factor determining work. Given the observed limitations of urinary osmolarity, increasing values of P would necessitate greater rates of urinary flow to produce maximum work. The actual relation between urinary flow and osmolarity, with the osmolarity decreasing with rising flow, is such that beyond a certain level of loading solute in the plasma, which is approximately 100 milliosmols/liter, maximum work can no longer be obtained, no matter how great the amount of loading substance administered. As a matter of fact, the work value may decrease, despite increasing urinary flows, loads, and plasma levels. These relationships serve to explain the failure to produce maximum work with either urea or sodium chloride. On the basis of the work equation and the observed relation between osmolarity and flow of the urine one may also determine by graphic methods the minimal urinary volume at which maximum work will be reached for any plasma level of loading solute under the simplifying assumption that the loading solute accounts for the entire urinary osmolarity.

Substituting the value of flow from equation 5 and using the identity $U = \frac{\text{load}}{\text{flow}}$, an equation is obtained in which both U and V are expressed in terms of load:

$$(7)\quad W = RT\ \text{load}\left(\frac{\ln A' e^{-k\ \text{load}} + B}{P} + \frac{P}{A' e^{-k\ \text{load}} + B} - 1\right),$$

in which the symbols have the same meaning as before. This equation permits one to relate directly work and solute load, and, by definition, urinary volume, for any given plasma level of loading solute on the same assumption as before, namely, that the loading solute accounts for the entire urinary osmolarity. One may also calculate the minimal urine volume at which maximum work will be reached.

The studies of glucose diuresis in diabetic subjects, beyond offering an explanation of the polyuria of diabetes, have a bearing on the problem of the cause of electrolyte loss during uncontrolled glycosuria. It was found that the urinary losses of sodium and chloride increased 4-fold above control levels during glucose diuresis, whereas the potassium losses were unchanged. Urea diuresis, on the other hand, did not affect the rate of electrolyte excretion.

At present studies are planned on the osmotic limitations and the work of the kidney at the other extreme of the osmotic relationships, *i.e.* during diuresis of water loading when the work of electrolyte conservation is at maximum.

Details of the foregoing studies will be published shortly.

References

1. Borsook, H., and Winegarden, H. M. *Proc. nat. Acad. Sci., Wash.*, 1931, **17**, 3.
2. Dresser, H. *Arch. exp. Path. Pharmakol.*, 1892, **29**, 303.
3. Galeotti, G. *Arch. Physiol.*, 1902, 200.
4. Gamble, J. L. *Proc. Amer. phil. Soc.*, 1944, **88**, 151.
5. Korányi, A. *Z. klin. Med.*, 1897, **33**, 1; 1898, **34**, 1.
6. McCance, R. A. *J. Physiol.*, 1945, **104**, 196; Hervey, G. R., McCance, R. A., and Tayler, R. G. O. *Proc. physiol. Soc.*, 1946, **104**.
7. Newburgh, J. D. *J. clin. Invest.*, 1943, **22**, 439.
8. Rhorer, L. *Arch. ges. Physiol.*, 1905, **109**, 375.

Effects of the Antithyrotoxic Factor of Liver on Growth and Survival of Immature Rats Fed Massive Doses of Thyroactive Materials[1]

B. H. Ershoff and H. B. McWilliams

Emory W. Thurston Laboratories, Los Angeles, and Department of Biochemistry and Nutrition, University of Southern California, Los Angeles

Available data indicate that liver contains one or more factors other than the known B vitamins that prolonged survival and counteracted the growth retardation of immature rats fed massive doses of desiccated thyroid

TABLE 1

Dietary component	Diet A	Diet B
Extracted liver residue*	0.0	10.0
Casein†	22.0	22.0
Salt mixture‡	4.5	4.5
Sucrose	73.5	63.5

To each kilogram of the above diets were added the following synthetic vitamins: thiamine hydrochloride, 72 mg; riboflavin, 9 mg; pyridoxine hydrochloride, 15 mg; calcium pantothenate, 67.2 mg; nicotinic acid, 60 mg; 2-methyl-naphthoquinone, 5 mg; and choline chloride, 1.2 gm. (In view of the increased requirements for thiamine, pyridoxine, and pantothenic acid in the hyperthyroid rat (*2*), the B vitamins in the present experiment were administered in excessive amounts in order to assure an adequacy of these factors in the diet.) Each rat also received 3 times weekly the following supplement: cottonseed oil (Wesson), 500 mg; *a*-tocopherol acetate, 1.5 mg; and a vitamin A-D concentrate (Nopco Fish Oil Concentrate, assaying 800,000 U.S.P. units of vitamin A and 80,000 U.S.P. units of vitamin D/gm) containing 50 U.S.P. units of vitamin A and 5 U.S.P. units of vitamin D.

* Extracted Liver Residue, Wilson Laboratories, Chicago, Illinois.

† Vitamin Test Casein, General Biochemicals, Inc., Chagrin Falls, Ohio.

‡ Salt Mixture No. 1 (*6*).

(*1, 3, 4*). Since liver feeding did not prevent the rise in oxygen consumption following thyroid administration (*3*), the question arises whether liver actually exerts an antithyrotoxic effect or whether it might not be counteracting other noxious substances present in the desiccated

[1] Communication No. 194 from the Department of Biochemistry and Nutrition, University of Southern California.

thyroid material. The present experiment was accordingly undertaken to determine the effects of the "antithyrotoxic factor" of liver on growth and survival of immature rats fed massive doses of thyroid, thyroxin, thyroglobulin, and iodinated casein.

Two basal rations, diet A and diet B, were employed (Table 1). Diet A was a purified ration containing the B-complex factors in synthetic form only. Diet B was similar in composition but contained Extracted Liver Residue (Wilson) in addition to the synthetic vitamins. ments were added in place of an equal amount of sucrose. One hundred and twelve female rats of the Long-Evans strain were selected at 21–23 days of age and with an average weight of 42.4 gm. These were kept in metal cages with raised screen bottoms to prevent access to feces and were fed the above diets *ad libitum*. Feeding was continued for 8 weeks or until death, whichever occurred sooner. Results are summarized in Table 2.

Findings indicate that the beneficial effect of Extracted Liver Residue on growth and survival of immature rats

TABLE 2

EFFECTS OF THE ANTITHYROTOXIC FACTOR OF LIVER ON GROWTH AND SURVIVAL OF IMMATURE RATS FED MASSIVE DOSES OF THYROID, THYROXIN, THYROGLOBULIN, AND IODINATED CASEIN

Dietary group	Thyroactive supplement	No. of rats	Initial body wt	Gain in body wt (gm) on following days of experiment:				Avg. survival time* (days)
				14th	28th	42nd	56th	
A	Desiccated thyroid	10	42.4	33.0 (6)†	61.0 (3)	87.5 (2)	97.5 (2)	28.2 ± 5.2
B	" "	10	42.5	51.8 (9)	96.4 (8)	123.8 (8)	136.4 (5)	49.4 ± 3.3
A	Thyroxin	10	42.0	29.9 (9)	57.3 (6)	70.7 (6)	80.7 (3)	37.5 ± 5.1
B	"	10	42.0	56.9 (10)	109.0 (10)	137.7 (10)	150.3 (10)	56.0 ± 0.0
A	Thyroglobulin	10	42.5	33.4 (9)	53.6 (7)	68.5 (2)	75.5 (2)	35.1 ± 4.0
B	"	10	41.9	58.8 (10)	109.3 (10)	132.1 (10)	145.4 (5)	51.7 ± 1.4
A	0.25% iodinated casein	10	43.1	30.0 (7)	33.3 (3)	57.0 (1)	....	22.6 ± 3.5
B	" " "	10	42.8	58.7 (9)	91.8 (5)	117.6 (5)	115.0 (1)	36.3 ± 4.4
A	0.5% iodinated casein	10	42.3	24.0 (7)	48.7 (3)	60.0 (2)	....	24.5 ± 4.2
B	" " "	10	42.3	46.3 (9)	90.5 (4)	116.5 (4)	113.0 (2)	35.9 ± 5.1
A	None	6	42.5	52.2 (6)	90.4 (6)	125.7 (6)	143.3 (6)	56.0 ± 0.0
B	"	6	42.3	63.0 (6)	107.0 (6)	137.3 (6)	154.8 (6)	56.0 ± 0.0

* Averages, computed on the basis of a 56-day survival time for animals alive at the termination of the experiment, include standard errors of the mean.

† Values in parentheses indicate number of animals that survived of which this is an average.

Recent work from this laboratory (*3*, *5*) indicates that the above material, consisting of the coagulated, water-insoluble material remaining after removal of the extractable water-soluble substances, is a potent source of "antithyrotoxic factor." Each of the above diets was supplemented with U.S.P. desiccated thyroid,[2] thyroxin,[3] thyroglobulin,[4] or iodinated casein.[5] Supplements were incorporated in the basal rations at the following levels: thyroid, 0.5%; thyroxin, 50 mg/kg of diet; thyroglobulin, 0.1%; and iodinated casein, 0.25% and 0.5%. Supplefed massive doses of desiccated thyroid is equally evident in rats fed massive doses of thyroxin, thyroglobulin, or iodinated casein. Effects were particularly striking in the thyroxin series, with a 100% survival over an 8-week period on diet B in contrast to a 30% survival on diet A; similarly, animals gained approximately twice as much weight on diet B as they did on diet A. Results were somewhat less marked in the iodinated casein series, possibly because of the greater thyroxin content of these rations.

[2] Thyroid Powder, U.S.P., Armour & Company, Chicago, Illinois.

[3] Thyroxin (Synthetic Cryst.), Roche-Organon, Inc., Nutley, New Jersey. The material was dissolved in .1 N NaOH, adjusted to pH of 8.0, and diluted to a volume containing 50 mg in 12.5 cc.

[4] Endothyrin, Harrower Laboratories, Glendale, California, a commercially prepared, partially purified thyroid preparation containing 0.995% total iodine.

[5] Protamone, Cerophyl Laboratories, Kansas City, Missouri.

References

1. BETHELL, J. J., WIEBELHAUS, V. D., and LARDY, H. A. *J. Nutrition*, 1947, **34**, 431.
2. DRILL, V. A., and OVERMAN, R. *Amer. J. Physiol.*, 1942, **135**, 474.
3. ERSHOFF, B. H. *Arch. Biochem.*, 1947, **15**, 365.
4. ERSHOFF, B. H. *Proc. Soc. exp. Biol. Med.*, 1947, **64**, 500.
5. ERSHOFF, B. H. *Exp. Med. Surg.*, in press.
6. SURE, B. *J. Nutrition*, 1941, **22**, 449.

Comments and Communications

Cytochrome C Labeled With Radioactive Iron

The production and use of tagged hemoglobin has become almost a routine procedure. To our knowledge, no attempt has been made to label related hemoproteins. By supplementing iron-depleted young rats with radioactive iron during the period of rapid growth, we were able to isolate from the tissues of these animals cytochrome C showing an activity of $1,235 \pm 9$ cpm for 1 mg of pure cytochrome C on a molecular-weight basis of 13,000. Radioactive iron of high specific activity (Fe^{55}) is used. Counts are taken by means of an argon-filled Geiger tube with a 1-mm beryllium window. Cytochrome C is isolated from heart and skeletal muscle according to the method of D. Keilin and E. F. Hartree (*Proc. roy. Soc. Lond.*, 1937, **B122**, 298). The catalytic activity of the isolated material in the succinoxidase test is high. Injected intravenously into rats, it is as well tolerated as commercial 85% pure cytochrome C. Special attention was given as to the presence of noncytochrome iron: (1) The spectral purity of our cytochrome C preparation is satisfactory, as the ratio of the extinction value at 550 mμ to that at 535 mμ for reduced cytochrome C and the ratio of the extinction value at 550 mμ for reduced to that of oxidized cytochrome C do not deviate more than 2% from the theoretical ratios; (2) the iron content of the preparation can be fully accounted for by cytochrome C since for 1 mg of pure cytochrome C, as indicated by spectrophotometric analysis, 4 $\mu g \pm 5\%$ of iron was found; and (3) hemoglobin, which is expected to carry the highest radioactivity in the experimental animals, has an activity not considerably higher than that of cytochrome C. Four μg of hemoglobin-iron assayed $1,584 \pm 10$ cpm, so small amounts of admixed hemoglobin, undetectable by spectrophotometric and iron analyses, can therefore not cause any appreciable part of the activity found in the cytochrome preparation.

The radioactivity finally present in the animals certainly reaches the border line of safety, but so far no deleterious effects have been observed. Reproduction and lactation seem unimpaired.

The total dose of radioactive iron injected into the animals used for the cytochrome preparation was about 11 mg. About 80% of the cytochrome-iron and 90% of the hemoglobin-iron are derived from this injected iron. Assuming 14 mg of total cytochrome C, corresponding to 60 μg of iron, for a 250-gm rat (M. W. Crandall and D. L. Drabkin. *J. biol. Chem.*, 1946, **166**, 653), about 0.45% of the injected dose is incorporated into cytochrome C, and assuming 3 gm of hemoglobin, corresponding to 10 mg of iron, about 80% of the injected dose is incorporated into hemoglobin.

Considering the radioactivity of the cytochrome C preparation, 1/500 of the usual 5-mg dose injected into rats should still be detectable. We hope this will enable us to trace the metabolic fate of injected cytochrome C and to attack the question of its actual penetration into tissue cells.

HELMUT BEINERT
and HEINZ MAIER-LEIBNITZ
USAF School of Aviation Medicine,
Randolph Air Force Base, Texas

Comparative Data on Vitamin B_{12} From Liver and From a New Source, *Streptomyces griseus*

The isolation from liver of crystalline vitamin B_{12} (E. L. Rickes, *et al. Science*, April 16, p. 396), a substance active in controlling the hematological (R. West, *Science*, April 16, p. 398) and probably the neurological (L. Berk, *et al. New Eng. J. Med.*, 1948, **239**, 328–330) manifestations of addisonian pernicious anemia, has been reported. The natural vitamins may occur in numerous and diverse animal, plant, and microbiological materials, and it was possible that sources of vitamin B_{12} other than liver could be found. Thus, several materials having growth-promoting activity for *Lactobacillus lactis* have been recorded by Shorb (*Science*, April 16, p. 397). As part of our research program on the distribution of this vitamin, numerous source materials have been investigated, and several have been found to show *L. lactis* activity. These include milk powder, beef extract, and culture broths of strains of *Mycobacterium smegmatis*, of *Lactobacillus arabinosus*, of *Bacillus subtilis*, and of several *Streptomyces* species, such as *S. roseochromogenus*, *S. griseus*, and *S. antibioticus*. The properties of a red crystalline compound which has been isolated from one of these, a grisein-producing strain of *S. griseus*, have been compared with those of vitamin B_{12}.

When heated on the micro-stage, the crystals lost their red color at about 212° and did not melt up to 320°. Crystalline B_{12} similarly darkened to black at 210–220° and did not melt below 300°. The crystals, after drying, were found to have refractive indices of 1.619 (α), 1.649 (β), and 1.659 (γ), which are in agreement with indices of 1.616 (α), 1.652 (β), and 1.664 (γ) for vitamin B_{12}. Emission spectrographic analysis of the crystals revealed the presence of cobalt and phosphorus, as it did for crystalline B_{12} (E. L. Rickes, *et al. Science*, August 6, p. 134). Solubility tests showed that the crystals and crystalline B_{12} have approximately the same solubility in 80% acetone, and that the addition of crystalline B_{12} to a saturated solution of the crystals in 80% acetone did not lead to a significant change in the concentration of the supernatant solution.

The crystals showed about 11.7×10^6 u/mg for the growth of *L. lactis* as compared with an average of 11×10^6 u/mg for crystalline B_{12}. They have shown optimal "animal protein factor" activity for the chick at a level of 30 μg/kg of diet, which is comparable with that found (W. H. Ott, *et al. J. biol. Chem.*, 1948, **174**, 1047) for vitamin B_{12}.

Randolph West has tested these crystals and found (personal communication) that the clinical response in pernicious anemia parallels that shown by vitamin B_{12}.

These comparative data are evidence that the crystals from the microbiological source and vitamin B_{12} are identical.

We wish to thank Dr. Charles Rosenblum for the determination of refractive indices and spectrographic analyses, and Mr. Frederick Bacher for the solubility measurements. We are indebted to Miss Muriel Caswell and her colleagues for the microbiological assays and to Dr. W. H. Ott for the determination of "animal protein factor" activity. We are indebted to Dr. H. B. Woodruff, Mr. David Hendlin, and Miss Myrle Ruger for collaboration on the extension of the research on the microbiological production of vitamin B_{12}.

EDWARD L. RICKES, NORMAN G. BRINK, FRANK R. KONIUSZY, THOMAS R. WOOD, and KARL FOLKERS
Research Laboratories,
Merck & Co., Inc., Rahway, New Jersey

Cultivation Is Necessary

The tremendous interest in the use of the various growth-regulating chemicals has brought forth imposing problems regarding unfavorable soil conditions in crop production. Inspection of a number of carrot fields in eastern Pennsylvania in 1947 revealed a very compact and unsatisfactory soil condition resulting from, among other things, a lack of satisfactory cultivation. This was due primarily to the lack of the necessity for cultivation to control weeds because of the use of certain weed-control substances. The yields were phenomenally low. It was believed that a part of this low yield was due to a lack of aeration and unsatisfactory soil conditions.

Experiments with carrots were designed in 1948 to study the influence of cultivation on the growth of the crop. These experiments were located on a Woodstown sandy loam at Cinnaminson, New Jersey, and on a Steinsburg silt loam near Newtown, Pennsylvania. One thousand pounds of a 5–10–10 fertilizer/acre was disked in after plowing in each case. Each of these experiments was carefully replicated 5 times and consisted of (1) hand-cultivation and hand-weeding and (2) no cultivation, with the use of oil spray and hand-weeding to control weeds. The following table gives the mean yield of carrots (lbs/acre):

Treatment	Steinsburg silt loam	Woodstown sandy loam
Cultivation and hand-weeding	11,658	11,126
Oil and hand-weeding and no cultivation	1,204	7,007

The above differences in yield were highly significant and leave no doubt that under the conditions of these experiments cultivation was a deciding factor in crop yield. Each of the uncultivated soils became extremely compact and unfavorable for root growth. It is realized that some cultivation is practiced by most growers, but in 1947 many soils in eastern Pennsylvania where carrots were grown became extremely compact, and the yields were low on these soils. The same was true to a lesser extent in 1948. Because of this fact and in view of the tremendous interest in chemical weed-control methods at this time, the above information is pertinent and warrants careful consideration by all concerned with crop production.

JACKSON B. HESTER and ROBERT L. ISAACS, JR.
Department of Agricultural Research,
Campbell Soup Company, Riverton, New Jersey

"Serology" and "Immunology"

In a recent communication (*Science*, October 8, pp. 377–378) M. S. Marshall discusses the uses of the terms immunology and serology and their interrelations. He pleads for "separation of the concept of immunity and the phenomena of serology." With much of what he says the writer is in agreement, for it long ago became evident that some of the content of "immunology" had nothing directly to do with immunity. In other words, "immunology" became a term of misrepresentation and was, therefore, contraindicated. The solution made was to take the newer term "serology" to refer to that branch of biology which deals with the nature and interactions of antigens and antibodies (A. Boyden. *Sigma Xi Quart.*, 1936, **24**, 154; *Physiol. Zool.*, 1942, **15**, 109). On this basis serology is the broad term referring to *all phases* of the nature and reactions of antigens and antibodies. Immunology should, then, properly be of a different kind of inclusiveness and refer to those matters, serological or otherwise, which relate to problems of immunity in organisms.

On this basis clarity and truthfulness of thought in both fields can be attained, and the human capacity to confuse with words to some extent held within limits. It would, moreover, be a great mistake to belittle serology and to attempt to restrict it to matters of the technique of handling antigens and antibodies, and nothing of this kind was the intent of Dr. Marshall's remarks. There is a distinct need for the broad term serology to cover the growing field of biology in which the nature and reactions of antigens and antibodies play their part. As in all other branches of biology, "observation and reflection" should go together and the term serology would include both. There has already developed a considerable body of fact, theory, and fundamental principle in serology and especially in systematic serology.

I commend Dr. Marshall for his critical analysis of the possible relation or lack of relation between immunity and serological reactions, and I trust that we will not sacrifice the gains already made in establishing serology as a broad term covering the nature and interactions of antigens and antibodies together with all the applications and implications of such knowledge. In this broad sense serology would include some phases of immunology and would overlap many other fields of biology, but so do genetics and evolution, and ecology, and all other biological subdivisions. However, each of these fields is to some extent distinctive in methods and results and entitled to a place in biology.

ALAN BOYDEN
Serological Museum, Rutgers University

Book Reviews

Man and his works: the science of cultural anthropology. Melville J. Herskovits. New York: Alfred A. Knopf, 1948. Pp. xviii + 678 + xxxvii. (Illustrated.) $6.75.

The appearance of a new general textbook in anthropology is always an event, for there have been fewer than a dozen in the entire history of the science. Of these, it is noteworthy that the work under consideration is the third to be published during 1948. Since each of the three is excellent in its own way, teachers of the subject will no longer suffer from a limited choice, nor lay readers from the lack of a sound introduction to a complex and rapidly expanding discipline.

The volume by Herskovits far surpasses its rivals, old and new, in its range. There is scarcely a subject with which cultural anthropologists have dealt, scarcely a problem with which they have wrestled, that does not receive attention. This leads the author into some fields hitherto unexplored in textbooks—for example, the techniques of field research. Such thoroughness and enterprise deserve praise, and the book is to be recommended to anyone who wants to gain a bird's-eye view of the entire field of cultural anthropology or to discover what its practitioners have been up to all these years.

The treatment throughout is catholic as well as comprehensive. All theoretical positions are presented and discussed with admirable fairness. Every book has the defects of its virtues, and this one is no exception. Range and an eclectic point of view have not been achieved without sacrifice. Few topics receive the meticulous analysis that the specialist demands. Live issues are too often glossed over, as in the following typical quotation (p. 237): "We . . . accept the insights each position affords us, without fully accepting any of them." Almost never does the discussion penetrate to the actual frontiers at which the science is being pressed forward today, much less offer suggestive glimpses into the unknown. To the professional anthropologist, therefore, and to other social scientists already moderately familiar with anthropology, the volume will be less informative and challenging than to the novice and the interested general reader.

GEORGE P. MURDOCK

Yale University

Methods in medical research. (Vol. I.) Van R. Potter. (Ed.) Chicago: Year Book Publishers, 1948. Pp. xiii + 372. (Illustrated.) $8.00.

This volume is a critical evaluation of important methods of investigation in four biomedical fields: (1) assay of antibiotics, (2) blood-flow measurements, (3) selected methods in gastrointestinal research, and (4) cellular respiration.

Forty-nine competent research men have contributed to the text in this valuable and useful enterprise. Research methods dealing with complex factors in health and disease call for perpetual scrutiny and re-evaluation. When this is done from time to time by competent investigations, both freshmen and seniors in medical research are aided in their work. They will welcome this volume, and subsequent volumes if they measure up to the standard set in Volume I.

A. J. CARLSON

University of Chicago

Foundations of psychology. Edwin Garrigues Boring, Herbert Sidney Langfeld, and Harry Porter Weld. (Eds.) New York: John Wiley; London: Chapman & Hall, 1948. Pp. xv + 632. (Illustrated.) $4.00.

This book is a substantial contribution to the textbook literature in psychology. The third edition of a book which first appeared (under another title) in 1935, it has profited by the experience with the two earlier ones. Consisting of 25 chapters by 19 authors, it has now grown to over 600 large pages of double-column text, twice the length of its first edition. It is an excellent job of bookmaking from cover to cover.

The changes in arrangement, to which the editors have no doubt given much thought, are of less importance than the changes in content because the chapters are independent enough to be rearranged by groups at the discretion of the instructor. Succinct characterization of the content is difficult. It is a conservative and conventional book in some respects, in that all the old material remains. The 168 pages devoted to sensation and perception, for example, probably contain about the same number of words as in the first edition, when those topics constituted a much larger fraction of the book. But the book is also a modern one because new topics, with a decidedly contemporary flavor, have been added to the old. Personality, social functions, and related topics occupied less than one-tenth of the first edition but now occupy nearly one-third of the book. There is even a chapter on vocational selection, an "applied" topic which would certainly have been foreign to the earlier editions. The presence of this chapter and material incorporated in other chapters reflects the vigorous experiences of psychologists in making use of their science during the war.

Teachers of psychology may react either favorably or unfavorably to the increase in length. To the extent that psychology courses last no longer than they formerly did, it is not possible to keep adding topics without subtracting, unless the coverage of each is less thorough. One answer is to devote more time to the subject. Whereas the older course may have covered one term only, a book of this kind is suitable for a full-year course. The other answer is for the teacher to select

ose materials which seem most appropriate to the urse he wishes to teach, leaving the remaining topics or more specialized courses.

Those in other scientific fields who wish to obtain a ound picture of contemporary psychology will find this ook a useful source. The annotated references at the nd of each chapter will serve them as they do the tudent.

In a field which is developing as rapidly as psychology it is just as well that we do not have an "official" textbook, but that we have a variety of books differing in length and emphasis. The distinguished list of authors and the wise and experienced editorship make this one of the authoritative textbooks.

ERNEST R. HILGARD

Stanford University

Scientific Book Register

ANDREWS, T. G. (Ed.) *Methods of psychology.* New York: John Wiley; London: Chapman & Hall, 1948. Pp. xiv + 716. (Illustrated.) $5.00.

CARLSON, ANTON J., and JOHNSON, VICTOR. *The machinery of the body.* (3rd ed.) Chicago: Univ. Chicago Press, 1948. Pp. xxi + 639. (Illustrated.) $4.50.

KROGER, F. A. *Some aspects of the luminescence of solids.* New York-Amsterdam-London: Elsevier, 1948. Pp. xi + 310. (Illustrated.) $5.50.

RIEHL, HERBERT, and CRESSMAN, GEORGE P. *Studies of upper-air conditions in low latitudes.* I: *On the formation of West Atlantic hurricanes* (Riehl); II: *Relations between high- and low-latitude circulations* (Cressman). (Victor P. Starr, Ed.) (Publ. Dept. of Meteorology, Univ. Chicago.) Chicago: Univ. Chicago Press, 1948. Pp. vi + 103. (Illustrated.) $2.00.

ROUSE, IRVING, and GOGGIN, JOHN M. (Eds.) *An anthropological bibliography of the Eastern seaboard.* (Eastern States Archeological Federation, Res. Publ. No. 1.) New Haven: The Federation, Yale Peabody Museum, 1947. Pp. 174. (Illustrated.) $2.50.

SARTRE, JEAN-PAUL. *The psychology of imagination.* New York: Philosophical Library, 1948. Pp. 285. $3.75.

SNODGRASS, R. E. *The feeding organs of Arachnida, including mites and ticks.* (Publ. 3944; Smithsonian Miscellaneous Collections, Vol. 110, No. 10.) Washington, D. C.: Smithsonian Institution, 1948. Pp. 93. (Illustrated.)

THOMPSON, GUY P. *Zoology laboratory studies (invertebrate and vertebrate).* St. Louis, Mo.: C. V. Mosby, 1948. Pp. 361. (Illustrated.) $4.25.

VALLEY, GEORGE E., JR., and WALLMAN, HENRY. (Eds.) *Vacuum tube amplifiers.* (Massachusetts Institute of Technology Radiation Laboratory Series.) New York-London: McGraw-Hill, 1948. Pp. xvii + 743. (Illustrated.) $10.00.

WELD, LEROY D. *A textbook of heat for upperclassmen.* New York: Macmillan, 1948. Pp. x + 437. $5.00.

WORTHEN, EDMUND L. *Farm soils: their management and fertilization.* (4th ed.) New York: John Wiley; London: Chapman & Hall, 1948. Pp. xiii + 510. (Illustrated.) $3.20.

WYCKOFF, RALPH W. G. *Crystal structures.* (Sect. I, 7 Chap.) New York-London: Interscience, 1948. (Looseleaf.) (Illustrated.) $8.00.

Just Received—

BLACK, PAUL H. *Machine design.* New York-London: McGraw-Hill, 1948. Pp. vii + 357. (Illustrated.) $4.00.

BOOTH, A. D. *Fourier, technique in X-ray organic structure analysis.* New York: Macmillan; Cambridge, Engl.: at the Univ. Press, 1948. Pp. ix + 103. (Illustrated.) $2.75.

DILLON WESTON, W. A. R., and TAYLOR, R. ERIC. *The plant in health and disease.* London: Crosby Lockwood, 1948. Pp. xii + 173. (Illustrated.) 21/.

DISERENS, LOUIS. *The chemical technology of dyeing and printing: vat, sulfur, indigosol, azo and chrome dyestuffs and their auxiliaries.* (2nd. ed.) (Trans. and rev. by Paul Wengraf and Herman P. Baumann.) New York: Reinhold, 1948. Pp. xxii + 500. $11.00.

DUNBAR, FLANDERS. *Synopsis of psychosomatic diagnosis and treatment.* St. Louis, Mo.: C. V. Mosby, 1948. Pp. 501. (Illustrated.) $6.50.

FIRTH, DOUGLAS. *The case of Augustus D'Esté.* New York: Macmillan; Cambridge, Engl.: at the Univ. Press, 1948. Pp. iii + 59. (Illustrated.) $1.75.

HENRICI, ARTHUR T., and ORDAL, ERLING J. *The biology of bacteria: an introduction to general microbiology.* (3rd ed.) Boston: D. C. Heath, 1948. Pp. xiv + 577. (Illustrated.) $5.50.

KNIGHT, R. L. *Dictionary of genetics: including terms used in cytology, animal breeding and evolution.* Waltham, Mass.: Chronica Botanica; New York: Stechert-Hafner, 1948. Pp. x + 183. $4.50.

PITTALUGA, GUSTAVO. *Vitaminas y sangre.* (Biblioteca del Medico Practico, Vol. XXV.) Havana: Cultural, S. A., 1948. Pp. xv + 746.

SADLER, WILLIAM S. *A doctor talks to teen-agers: a psychiatrist's advice to youth.* St. Louis, Mo.: C. V. Mosby, 1948. Pp. 379. $4.00.

WARKENTIN, JOHN, and LANGE, JACK D. *Physician's handbook.* (5th ed.) Palo Alto, Calif.: Univ. Medical Publishers, 1948. Pp. iv + 293. (Illustrated.) $2.00.

WOLFF, WERNER. *Island of death: a new key to Easter Island's culture through an ethno-psychological study.* New York: J. J. Augustin, 1948. Pp. 228. (Illustrated.) $7.00.

———. *Growth: in relation to differentiation and morphogenesis.* (Symposia of the Society for Experimental Biology, No. II.) New York: Acadamic Press, 1948. Pp. vi + 365. (Illustrated.) $7.50.

NEWS and Notes

Clarence Zener, professor of metallurgy at the Institute for the Study of Metals, University of Chicago, is serving as special lecturer and consultant in physical metallurgy in the Department of Mining and Metallurgical Engineering, University of Illinois.

Glenn Ray Noggle, formerly on the staff of Blandy Farm, University of Virginia, has been appointed senior biologist in the Biology Division of the Oak Ridge National Laboratory, Oak Ridge, Tennessee.

Hutton D. Slade, formerly with the Research Division of Wallerstein Co., Inc., and **Eugene L. Hess,** formerly research associate in the Department of Physical Chemistry, University of Wisconsin, have joined the staff of the Rheumatic Fever Research Institute at Northwestern University Medical School. Dr. Slade will continue his studies in bacterial physiology and metabolism, while Dr. Hess will conduct biophysical studies of tissues.

Benjamin Epstein, formerly at Carnegie Institute of Technology, and **Gerald Harrison,** lately of Queens College, have been appointed associate professor and assistant professor, respectively, in the Mathematics Department of Wayne University.

Allan G. Douglas, formerly professor of biology at Southwest Missouri State College, has accepted a position in the Biology Department at California State Polytechnic College.

Visitors to U. S.

W. A. Macfarlane has been loaned by the Ministry of Fuel and Power to the Department of Scientific and Industrial Research for appointment as director of the United Kingdom Scientific Mission in the British Commonwealth Scientific Office in Washington, D. C. He will also serve as attaché for scientific questions in the British Embassy. The present director, **F. N. Woodward,** will return to the United Kingdom toward the end of the year.

Li-chi Tai, who is associated with the Iron and Steel Division of the Chinese National Resources Commission, Nanking, is taking a 6-month postgraduate course at the Carnegie Institute of Technology on a grant from a $25,000 fund provided by the American Chemical Society through UNESCO for the purpose of assisting foreign students. Dr. Tai is the fourth student to work under the grant, which was established two years ago.

M. Gerard Dreyfuss, French engineer, is now studying at the Harvard School of Engineering under a fellowship. A graduate of the Ecole Nationale des Ponts et Chaussées, the oldest engineering school in Europe, he is taking up at Harvard the study of soil mechanics and foundations.

Grants and Awards

Upon recommendation of the National Advisory Mental Health Council, the Surgeon General of the Public Health Service has been authorized to make grants for research in the field of mental health for periods beyond the fiscal year 1949. If approved during the fiscal year 1949, they will constitute a contractual obligation of the Government to forward finance the research projects beyond the present fiscal year. Forward financing of grants to medical schools for undergraduate training in mental hygiene was also authorized, but obligations for both research and training grants must not exceed $2,300,000. This limit will not permit forward financing of all mental health grants, and some will continue under the old system. The institutions and individuals to benefit from the new arrangement will be determined at a meeting of the Council this month.

The Department of Pharmacology of Baylor University College of Medicine, Houston, has obtained grants for the following studies: from the Bilhuber-Knoll Corporation, $2,250—cardiovascular effects of some aliphatic amines; from the Lakeside Laboratories, $500 and equipment valued at $1,500—fundamental mechanisms involved in mercurial diuresis; and from the U. S. Public Health Service, $8,650—kidney function.

Marcelle V. Schubert, Triple Cities College of Syracuse University, Endicott, New York, has received a Frederick Gardner Cottrell grant of $1,950 from the Research Corporation for research on "Crystallization of Yeast Invertase."

The Alexander Agassiz gold medal and honorarium for 1948 was awarded to Thomas Gordon Thompson at the autumn meeting of the National Academy of Sciences held at the University of California, Berkeley. Dr. Thompson, who is professor of chemistry and director of the Oceanographic Laboratories of the University of Washington, has long been a leader in investigations of the complex chemistry of the ocean and has participated very actively in international oceanographic research. Established by Sir John Murray in 1911, the medal is awarded by the Academy "for original contribution in the science of oceanography to scientific men in any part of the world."

The 1948 Scientific Award of the Grocery Manufacturers of America has been conferred on George R. Cowgill, professor of nutrition at Yale University. Dr. Cowgill, who received the award during the organization's annual meeting in New York City last month, was cited for "his fundamental contributions to the science of nutrition, particularly his research on the functional role of vitamin B_{12}, his success as a teacher of young biochemists, and his outstanding editorial work for the *Journal of Nutrition.*"

Brig. Gen. Edgar Erskine Hume received the Gorgas Award of Wyeth, Inc., at the recent annual dinner of the Association of Military Surgeons in San Antonio, Texas. He was cited for halting Naples' wartime typhus epidemic by the first mass-scale use of DDT and for his general advancement of preventive medicine since entering the Medical Corps in 1916.

Vladimir K. Zworykin, vice-president and technical consultant of the RCA Laboratories Division, Princeton, New Jersey, has been named winner of the 1948 gold medal of achievement of the Poor Richard Club in recognition

his invention of the electronic scan-. He will receive the gold medal ceremonies in Franklin Institute, nuary 7.

olleges and Universities

A $20,000,000 scientific develop-ent program was approved last onth by the Committee on Financing velopment of the Massachusetts stitute of Technology Corporation. bout half of the amount required will assigned as endowment and unre-icted funds, the balance being in-sted in new buildings and equipment. me of the new buildings planned ill be laboratories for nuclear science d engineering, metals processing, ology and food technology, hydro-namics, and electronics.

The Department of Geology and eography, University of Tennessee, sponsoring a symposium on the min-al resources of the Southeast which ill be held on the Knoxville campus arch 3–5, 1949. According to Frank Snyder, chairman of the symposium mmittee, papers on the major metal-ic and nonmetallic mineral products the Southeast will be presented by vited speakers.

A joint program of clinical cancer esearch has been announced by W. A. Bloedorn, dean of George Wash-ngton University Medical School, nd J. R. Heller, Jr., director of the National Cancer Institute. A com-mittee to develop and direct the new program has been appointed with Roy Hertz, assistant professor of medicine t George Washington and chairman f the Endocrinology Section of NCI, s chairman. The cooperative pro-gram, financed from the University's ancer research funds, which come rom grants made by NCI, the Amer-ican Cancer Society, and private ources, will initially devote atten-tion to (1) endocrine and metabolic spects of cancer of the breast, pros-tate, uterus, ovaries, and testes, in-cluding possible use of hormone ther-apy; (2) studies in nutritional as-pects of cancer of the gastrointes-tinal tract; and (3) study of meta-bolic aspects of nitrogen-mustard therapy in lymphoid diseases. A clin-ical laboratory for these studies has been set up at the new George Wash-ington Hospital, and additional facili-ties will be provided by NCI.

The losses suffered by the Depart-ment of Botany at the University of Kentucky on November 12 when fire almost totally destroyed Norwood Hall, in which it was housed, have been reported to *Science*. The entire herbarium of approximately 30,000 plants and most of the equipment were completely destroyed. An ad-joining greenhouse was badly dam-aged, and most of the plants in it, including several thousand research seedlings, were killed by heat. Wayne C. Hall, Frank T. McFarland, and B. B. McInteer, members of the Bot-any staff, lost all personal material kept in the building, their collections, and libraries, one of which contained several thousand books. While the office of Herbert P. Riley, head of the Department, was not burned, a num-ber of books in it were damaged by water. Much valuable material was also lost by the Kentucky Geological Survey and the State Department of Mines, which shared the building.

A 20,000,000-volt betatron, now being constructed at the University of Cincinnati from less than $2,000 worth of war surplus and other mate-rials, will, upon completion early in 1949, be the starting point from which the University will launch a large-scale atomic energy program. When the project was conceived two years ago, Francis Jankowski, a graduate student in the Applied Sci-ence Research Laboratory of the Uni-versity, was assigned to drawing the plans. In addition to designing the betatron, he has done much of the actual building under the direction of Walter Soller, head of the Labora-tory. To gain additional experience for the assignment, Mr. Jankowski worked in the Argonne National Lab-oratory, where he developed a method for measuring the intensities of the neutron beams used in atomic energy research. The project was assisted by donations of magnetic iron from a Cincinnati firm and the main vacuum tube from the University of Illinois.

A miniature supersonic wind tun-nel, simulating flying conditions of 1,360 mph at an altitude of 80,000′, has been put into operation at the University of Washington Aeronauti-cal Laboratory, Seattle. The com-plete unit, measuring 20′ long and 4′ high, has a test section of only 1″×2″. It is the first of its size to be designed with an enclosed air-stream system, which cleans and drys the air while returning it for reuse, thus making it unnecessary continu-ally to remove moisture from outside air. The tunnel maintains an air-stream speed three times the speed of sound, achieving a Mach number of three—or an air-stream velocity three times the speed of sound at −250° F. Modifications will be added to allow tests approximating actual conditions at an altitude of 200,000′ with an air-stream speed of 2,000 mph.

G. E. Ledbetter, who began work on the tunnel in 1946 as a research fellow, and D. W. Lueck, research engineer of the University Engineer-ing Experiment Station, are in charge of the project. They are now constructing a second tunnel with a 3″×3″ test section, which will be completed in January.

Industrial Laboratories

General Electric's traveling exhibit of electrical measuring devices, called the "Carnival of Measurements," will be viewed in 80 major U. S. industrial cities. Featured in the display is the new GE I-50 watt-hour meter, the rotating disk and shaft of which are suspended in space by the interaction of two tiny magnets. Various other devices include aircraft instruments, photometric devices, telemeters, etc. The tour will be completed in July of next year, when the exhibit may be seen in the New York area.

Kenneth C. D. Hickman, inventor of the modern molecular still used for refining heat-sensitive oils, has en-tered into an arrangement by which he will divide his time between the Eastman Kodak Company, Rochester, New York, and Arthur D. Little, Inc., Cambridge, Massachusetts. While serving on the staff of the latter, he will do research in a field of high-vacuum engineering not previously commercially developed and be avail-able for general consultation.

Meetings and Elections

The Maryland Chapter of the Society of the Sigma Xi will meet at 8:00 P.M., December 13, in the Agriculture Building of the University of Maryland, College Park. Walter N. Ezekiel, head mycologist in charge of moisture and fungus proofing, Bureau of Ordnance, Navy Department, will speak on "Problems of Deterioration of Military Equipment." The meeting will be open to the public.

The American Anthropological Association, American Folklore Society, and **Society for Applied Anthropology** will meet at the Royal Ontario Museum of Archaeology and the University of Toronto on December 28–30. General sessions will be devoted to archaeology, personality and culture, acculturation, education, theory, diffusion, language and culture, physical anthropology, and methods. A special meeting, sponsored by the Society for Applied Anthropology and under the chairmanship of G. Gordon Brown, will include the following papers: "Administration of Indians," "Some Experiments in Culture Change," "Causes and Effects of Migration of British Columbia Indians to Washington Berry Fields," and "A Study in the Problems of Re-education in Industry." A panel discussion on "The Adjustment of the Canadian Indian" will follow. Another feature of the meeting will be a symposium on "The Contributions of Community Studies in Anthropology," with Conrad M. Arensberg presiding. Further information may be obtained from the secretary of the Association, D. B. Stout, Department of Sociology and Anthropology, Syracuse University, Syracuse 10, New York.

The American Society for X-Ray and Electron Diffraction (ASXRED) will hold a combined business meeting and scientific session December 16–18 at the Battelle Memorial Institute, Columbus, Ohio. A symposium on "Identification of Materials by Crystallographic Means" will be a feature of the meeting. Those planning to attend should communicate with C. M. Schwartz, of the Batelle Memorial Institute.

The Optical Society of America is planning a Symposium on Luminescence as a feature of its winter meeting to be held in New York City on March 10–12, 1949. One day of the general meeting will be devoted to this symposium. Those working on luminescence are invited to participate in it, whether or not they are members of the Society. Plans for the symposium will be facilitated if those desiring to contribute will communicate as early as possible with Dr. Gorton R. Fonda, Research Laboratory, General Electric Company, Schenectady, New York.

The Southeastern Branch of the Society of American Bacteriologists held its third biannual meeting October 22 at the University of Georgia, Athens, with representatives from Florida, Alabama, and Georgia attending. Martha J. Johnson, secretary-treasurer, reports that the meeting was called to order by W. C. Burkhart, president of the Branch and head of the Bacteriology Department at the University of Georgia. George H. Boyd, dean of the Graduate School welcomed members and guests. Fourteen papers were presented. At a banquet held at the Holman Hotel, W. F. Friedewald, chairman of the Department of Bacteriology at Emory University Medical School, spoke on "Virus and Host Cell Relationships."

The spring meeting will be held in Knoxville, Tennessee, as a joint meeting with the Kentucky-Tennessee Branch, the Association of Southeastern Biologists, and the Southeastern Section of the Botanical Society.

The 8th General Assembly of the International Scientific Radio Union, held in Stockholm, Sweden, July 12–20, was attended by 100 persons. A total of 153 scientific papers had been submitted for the meeting. Most of these were presented by abstract, but some were presented in full, and grouped by topics. These led to lively discussions. The scientific sessions were organized under the Union's four "Commissions": (1) Radio Standards and Methods of Measurement; (2) Radio Propagation; (3) Radio Noise; (4) Radio Physics.

The work of the Commissions led to new plans for international cooperation in scientific radio research, including the intercomparison of standards for the measurement of field intensity, joint studies of standard sources of radio noise and of radio-frequency power measurement, and researches on interaction of radio waves, tidal phenomena in the ionosphere, tropospheric propagation, and nonlinear oscillations.

The newly elected officers of the Union, for a term of office extending to the next General Assembly, are: president, Sir Edward Appleton (England); vice-presidents, J. H. Dellinger (U.S.A.), B. van der Pol (Holland), H. Sterky (Sweden), R. P. Lejay (France), J. Lugeon (Switzerland), and Col. A. E. Dorsimont (Belgium); treasurer, C. H. Manneback (Belgium); secretary, E. Herbays (Belgium). R. Bureau, head of the French National Radio Laboratory, was made an honorary president of the Union.

The business affairs of the Union were reorganized, largely as a result of recent action taken by UNESCO to participate in financial support of the Union. A representative of UNESCO was in attendance at the General Assembly. The technical Commissions of the Union are to be more active, and certain expenses of their officers in attending meetings will be paid by the Union. Separate English and French versions of all documents, instead of the unsatisfactory polyglot documents of the past, will be issued after this year.

The number of technical Commissions was increased. The Commissions and their chairmen are as follows: Radio Standards and Methods of Measurement — J. H. Dellinger (U.S.A); Tropospheric Radio Propagation—C. R. Burrows (U.S.A.); Ionospheric Radio Propagation—Sir Edward Appleton (England); Terrestrial Radio Noise—H. Norinder (Sweden); Extraterrestrial Radio Noise—D. F. Martyn (Australia); Radio Waves and Circuits, including General Theory and Antennas—B. van der Pol (Holland); and Electronics, including Properties of Matter—G. Lehmann (France).

Representatives of the Union were appointed to serve on three Joint Commissions established by this and

ther Unions, all organized under the International Council of Scientific Unions. The Joint Commissions are on: Ionosphere, Radio-Meteorology, and Terrestrial and Solar Phenomena. The members from the United States are, respectively, N. Smith, C. R. Burrows, and D. H. Menzel.

Members of the American delegation attending the Stockholm meeting were: J. H. Dellinger (chairman of delegation), chairman of U.S.A. National Committee; W. B. Burgess, Naval Research Laboratory; C. R. Burrows, director, College of Engineering, Cornell University; F. T. Davies, chief, Radio Propagation Laboratory, Ottawa, Canada; K. R. Eldredge, Office of Naval Attaché, London; Lt. Col. C. W. Janes, U.S.A. Signal Corps; K. Lark-Horovitz, head of Physics Department, Purdue University; F. B. Llewellyn, Bell Telephone Laboratories; H. O. Peterson, Riverhead Laboratory, Radio Corporation of America; P. F. Siling, Engineer in Charge, RCA Frequency Bureau; and Newbern Smith, Central Radio Propagation Laboratory, National Bureau of Standards.

The next General Assembly will be held in Switzerland, probably in Zurich, in 1950. (J. H. DELLINGER, *Chairman, U.S.A. National Committee.*)

The American Institute of Chemical Engineers, at its recent annual meeting in New York City, elected the following officers: Francis J. Curtis, of the Monsanto Chemical Company, St. Louis, president; Warren Lee McCabe, of the Flintkote Corporation, vice-president; and, as directors, H. D. Wilde, Humble Oil and Refining Company; Paul D. V. Manning, of the International Mineral and Chemical Corporation; Donald B. Keyes, of the Heyden Chemical Corporation; and Irvin L. Murray, of Carbide and Carbon Chemicals Corporation.

NRC News

Ralph E. Cleland, head of the Department of Botany, University of Indiana, has been appointed chairman of the Division of Biology and Agriculture. New executive secretary of the Division and also of the American Institute of Biological Sciences is **Milton O. Lee.** Dr. Lee is also secretary of the Federation of American Societies for Experimental Biology as well as executive secretary of the American Physiological Society.

An American Geological Institute, comprising 11 national societies with a combined membership of more than 10,000 professional geologists, has been organized to direct the talents of the profession into more effective channels of national service. The Institute will be sponsored by the National Research Council. The first meeting of the directors, named by the affiliated societies, was held November 15–16 in Washington, D. C., to initiate immediate action in speeding the discovery of additional reserves of scarce materials, the detailed geologic mapping of the United States, greater recognition and use of geologists and the geologic sciences in governmental agencies and the armed services, the training of more geologists in colleges and universities to overcome the present critical shortage within the mineral industries, the improvement of educational standards in the geologic sciences, more effective dissemination of geologic research information, and greater public understanding and appreciation of the role of geology in modern civilization.

Officers of the new Institute are: A. I. Levorsen, dean of the School of Mineral Sciences, Stanford University, president; Wm. B. Heroy, consulting geologist and geophysicist of Dallas, Texas, vice-president; and Earl Ingerson, of the U. S. Geological Survey, Washington, D. C., secretary-treasurer. The member societies include the Geological Society of America, American Association of Petroleum Geologists, American Institute of Mining and Metallurgical Engineers, American Geophysical Union, Mineralogical Society of America, Society of Economic Geologists, Society of Exploration Geophysicists, Society of Economic Paleontologists and Mineralogists, Seismological Society of America, Paleontological Society, and Society of Vertebrate Paleontology.

Headquarters will be established at the National Academy of Sciences, Washington, D. C., as soon as an executive secretary has been appointed.

Deaths

Arthur J. Wilson, 64, head of the Chemistry Department, North Carolina State College, died November 11 in Raleigh, North Carolina, as the result of a heart attack.

Samuel T. Orton, 69, authority on speech disorders, died November 17 in St. Francis Hospital, Poughkeepsie, New York. He had recently retired as professor of neurology and neuropathology at the College of Physicians and Surgeons, Columbia University.

John E. Goodwin, 73, head librarian, University of California at Los Angeles, died November 18 in Santa Monica, California.

Excavation of a prehistoric Eskimo village on the shores of Frobisher Bay, Baffin Island, in the Canadian Arctic, has yielded artifacts of two ancient cultures. The archaeological stury was undertaken this summer by Henry B. Collins, Jr., of the Smithsonian Institution, and Colin Thacker, of the National Museum of Canada (see *Science,* July 9, p. 36). The village consisted of one-room houses of stone and whalebone built in excavations about two or three feet deep with roofs above the surface. The houses were entered by subterranean passageways. One of the dwellings, showing the stones of the passageway in the foreground, is pictured on this week's cover. Most of the artifacts were typical of the Thule culture, which is thought to have originated in Alaska and spread eastward along the Arctic coasts about 800 years ago. Some found on Baffin Island are almost identical to those of the same period in Alaska, indicating that the migration may have have occurred over a short period of time, possibly only one generation. Underlying and mixed with these, however, were found a number of small, delicately carved implements which belong to the Dorset culture. The latter shows resemblance to the oldest Eskimo artifacts found in Alaska which may have been the work of the earliest migrants from Asia. The village on Frobisher Bay has not been precisely dated, but it certainly preceded the

culture found there by Martin Frobisher, the 16th-century explorer, who found the Baffin Island Eskimo already using iron.

The 131-year-old New York Academy of Sciences recently opened a campaign for a $1,000,000 fund to finance the construction and maintenance of a permanent Academy building and science center in New York City. According to its president, Harden F. Taylor, the organization's present accommodations in the American Museum of Natural History are inadequate for its conference and publication activities. In the last 11 years, membership in the Academy has grown from 324 to 4,000. The organization plans to spend $500,000 to purchase and recondition a centrally located building and $500,000 to expand its program into the fields of astrophysics, mathematics, experimental medicine, and public health.

"Suggestions for Science Teachers in Devastated Countries," an illustrated booklet recently published by UNESCO, is now being distributed free to schools in Greece, Poland, Czechoslovakia, Austria, Hungary, Italy, China, and the Philippines. Its author, who is science master at the City of London School and member of the Royal Society Committee for Cooperation with UNESCO, explains how science teaching can be begun without apparatus and then how equipment for experiments in astronomy, meteorology, measurement, heat, light, magnetism, electricity, chemistry, and biology can be improvised from easily obtainable materials. In the Introduction the author emphasizes that the improvisations should not be considered makeshifts, but that they and their construction are in the best tradition of science and science teaching. Several useful sections are included on laboratory directions, charts, and logarithm tables, and mention is made of the use of visual aids in science teaching and recently developed laboratory materials. The most outstanding feature of the booklet, however, is the great number of concise diagrams accompanying the text. It has been suggested by UNESCO that teachers in more fortunate countries may find the booklet useful for extending the scope of classes at little cost.

Scientists wishing to send Christmas gifts of food to colleagues abroad may now select two new assortments through CARE—the Holiday Package ($15), including a whole turkey and other foods sufficient for a dinner for 12, and the Standard Food Package ($10), recently revised to contain more meats, fats, and sweets. The former may be sent to Austria, Belgium, Czechoslovakia, Finland, France, Germany (American, British, French Zones and all of Berlin), Great Britain (Scotland, Wales, and northern Ireland), Greece, Italy, Hungary, the Netherlands, and Poland; the second package may be sent to all of these countries with the exception of Poland, Great Britain, Greece, and Italy. There will be an additional charge for packages sent to Berlin during the blockade. Assortments of food designed to meet specific national tastes are also available for all countries previously mentioned and Japan, Okinawa, and Korea. Orders may be addressed to CARE, 50 Broad Street, New York City, or to local CARE outlets in major cities.

A lead chloride crystal measuring $2\frac{1}{2} \times 4$ cm, believed to be the largest ever grown, has been produced by Joseph M. Ashcroft and A. Smakula at the Engineer Research and Development Laboratories, Fort Belvoir, Virginia. This was done by lowering a melt of purified commercial lead chloride crystals in a glass crucible through a temperature gradient, in a specially designed furnace, at the rate of only 1.2 cm/day. This procedure was necessary to grow a single crystal instead of a mass of small crystals. The crystal will be subjected to optical and other physical tests impossible with the minute crystals available commercially.

Make Plans for—

Symposium on the Pathogenesis and Pathology of Viral Infections, December 14–15, New York Academy of Medicine, 2 East 103rd Street, New York City.

Mycological Society of America, December 26–30, Chicago, Illinois.

Botanical Society of America, Inc., December 27–30, Stevens Hotel, Chicago, Illinois.

National Science Teachers Association, December 27–30, Washington, D. C.

American Society of Plant Physiologists, December 27–31, Chicago, Illinois.

7th Pacific Science Congress, February 2–8, Auckland New Zealand; February 16–22, Christchurch.

Recently Received:

Blumea (*Tijdschrift voor de Systematiek en de Geografie der Planten*)—a journal of plant taxonomy and plant geography. Vol. VI, No. 1, pp. 1–336. Published by the Rijksherbarium, Leiden, Holland.

Collected papers of the Institute of Medical and Veterinary Science, Adelaide, South Australia, 1944–47, Vol. 3.

News Bulletin of the Institute of International Education, 2 West 45th Street, New York City 19.

Ultrafax: a high-speed radio communication system. Descriptive pamphlet issued by the Radio Corporation of America, 30 Rockefeller Plaza, New York City 20.

Statlab Review, a publication of the Statistical Laboratory, Iowa State College, Ames.

Bibionidae, by D. Elmo Hardy. (Ruwenzori Expedition, 1934–35, Vol. 1, No. 6.) London: British Museum of Natural History, 1948.

Journal of the New York Botanical Garden, November 1948.

An analysis of the real cost of TVA power, by C. J. Green. Published by the Natural Resources Department, U. S. Chamber of Commerce, Washington 6, D. C.

Annual Report of the Statistical Laboratory, Iowa State College (1947–48).

Guarding our wildlife resources, by Rachel L. Carson. (Conservation in Action, No. 5, illustrated.) Washington, D. C.: U. S. Government Printing Office, 1948. $.30.